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Application of Quantitative Models of Choice to Alcohol-Maintained Behavior

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APPLICATION OF QUANTITATIVE MODELS OF CHOICE TO ALCOHOL-MAINTAINED BEHAVIOR

by

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ABSTRACT

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Choice procedures and quantitative models of choice behavior have been used to assess the reinforcing efficacy of drugs. Few studies, however, have used quantitative models of choice for the study of behavior maintained by alcohol. In addition, no studies have assessed the usefulness of quantitative models of concurrent-chains performance for the study of drug-associated cues. The purpose of the present series of experiments was to test the generality of the matching law with alcohol as a reinforcer and extend the use of quantitative models of concurrent-chains performance to behavior maintained by alcohol and alcohol-associated cues. In the first experiment (Chapter 2), rats responded for an alcohol solution on concurrent variable-interval schedules of reinforcement. Across conditions, relative rates of alcohol reinforcement were varied, which allowed for estimates of the parameters of the generalized matching law. Overall, the matching law accounted for changes in rats' relative allocation of behavior with changes in the relative

rate of alcohol delivery. The second and third experiments (Chapter 3) extended the use of the concurrent-chains procedure to rats responding to gain access to stimulus contexts associated with different rates of alcohol delivery. These experiments examined whether initial-link preference would change as a result of changes in the relative rate of alcohol deliveries in the terminal links and whether increases in the initial-link schedules would result in a decrease in preference (i.e., initial-link effect), as predicted by models of concurrent-chains performance. Results showed that choice between two terminal links depended on the different rates of alcohol delivered in each terminal-link stimulus context. When the initial-link schedules were increased, preference for the preferred context decreased. Future studies can benefit from the use of quantitative models of behavior on concurrent and concurrent-chains schedules as a framework for the assessment of potential behavioral and pharmacological treatments of drug abuse and dependence.

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CHAPTER 1

INTRODUCTION

Drug abuse and dependence are important human problems that are characterized by a maladaptive pattern of persistent drug seeking and taking (American Psychiatric Association [APA], 1994). Drug self-administration procedures have been useful in the study of the variables that contribute to the maintenance of drug taking and for the study of the reinforcing effects of drugs in both human and animal research (Pickens, Meisch, & Thompson, 1978). As with any operant conditioning procedure, a specific response (e.g., pressing a lever) is followed by the delivery of a reinforcer (e.g., alcohol solution), which increases the probability of the behavior occurring in the future. Drugs typically operate like more conventional reinforcers (e.g., food), and the contingency between the response and reinforcer is critical in determining rates and patterns of responding.

The study of the reinforcing efficacy of drugs has been very useful in the design and interpretation of manipulations such as changes in access and dose of drug, access to an alternative nondrug reinforcer, or pharmacological treatments. Initially, the reinforcing efficacy of drugs was measured by the response rates a certain drug or dose maintained on simple schedules of reinforcement (e.g., fixed-ratio; see Griffiths, Brady, & Bradford, 1979; Katz, 1989, for reviews). A common finding is that, at lower doses, response rates increase with increases in drug dose, but response rates decrease with continued increases in drug dose (i.e., inverted-U function; e.g., Pickens & Thompson, 1968; Woods & Schuster, 1968; see Katz, 1989, for review). What this finding suggests is a decrease in the reinforcing efficacy of the drug with greater reinforcer magnitude. However, results

from other studies suggest that response rates are not an accurate index of the reinforcing efficacy of drugs (e.g., Dougherty & Pickens, 1973; Pickens & Thompson, 1968). Dougherty and Pickens showed that the inverted U-shaped function between drug dose and response rates was due to increases in postreinforcement pause as the drug dose increased. This increase in postreinforcement pause has been suggested to be a result of a general dose-related disruption of behavior (i.e., direct effects of the drug).

To circumvent the problem associated with response rates as a measure of the reinforcing efficacy of drugs, choice procedures have become more prevalent (e.g., Meisch, 2000; Woolverton, 1996). In choice procedures, concurrently available and independent schedules of reinforcement deliver different doses or rates of a drug reinforcer. The reinforcing efficacy of the drug is measured by preference for a response alternative. Preference is defined as relative time or amount of responding on each response alternative (Williams, 1988). An advantage of choice procedures is that preference provides a relative measure of behavior that is highly sensitive to reinforcement variables, resulting in orderly relations between behavior and reinforcement that allow for quantitative description (Williams). As a result, the reinforcing efficacy of drugs can be separated from their direct effects on behavior (i.e., disruption of response rates at higher doses).

Choice

The study of choice has been the focus of many investigations in the field of operant learning. The procedure typically used to study choice is known as a concurrent schedule of reinforcement. In this procedure, two or more independent responses are

concurrently available and responding on each alternative is maintained by an independent schedule of reinforcement (Ferster & Skinner, 1957). Variable-interval (VI) schedules are useful for quantitative analysis of choice because the obtained rate of reinforcement generally will be approximately equal to the programmed rate of reinforcement across a wide range of response rates. As a result, the experimenter can control the total number of reinforcers delivered in an experimental session. Control of the reinforcers delivered is important because a change in the experimental subject's behavior does not affect the independent variable (i.e., rate of reinforcement), as can occur with ratio schedules of reinforcement. Typical manipulations used in the study of choice include changes in relative rates of reinforcement (e.g., one VI schedule provides greater *frequency* of reinforcement than the other alternative) or changes in the magnitude of reinforcement (e.g., one alternative provides greater *quantity* of the reinforcer than the other alternative; see Davison & McCarthy, 1988, for review). Results obtained with these procedures typically are analyzed within the quantitative framework of the matching law.

The Matching Law

The matching law, proposed by Herrnstein (1961, 1970), states that the proportion of behavior allocated to one alternative matches the relative rate of reinforcement delivered for that alternative. In quantitative terms:

$$\frac{B_1}{B_1 + B_2} = \frac{R_1}{R_1 + R_2}, \tag{1}$$

where B represents responses per min, R represents reinforcers per min, and the

subscripts refer to the response alternatives.

Studies of choice using Equation 1, typically referred to as the strict matching law, have found systematic deviations from this equation (e.g., Staddon, 1968). In other words, organisms do not perfectly match their behavior to the relative rate of reinforcement delivered for each alternative. The existence of systematic deviations from the predictions of the model suggests that the model does not adequately account for the allocation of behavior.

The Generalized Matching Law

To account for the systematic deviations from strict matching, Baum (1974) proposed the *generalized matching law*. The generalized matching law is a power function, which in its logarithmic (log) version states that:

$$\log\left(\frac{B_1}{B_2}\right) = a\log\left(\frac{R_1}{R_2}\right) + \log b\,, \tag{2}$$

where *B* represents responses per min, *R* represents reinforcers per min, the subscripts refer to the response alternatives, *a* refers to *sensitivity* to relative rates of reinforcement, and log *b* refers to *bias*. In Equation 2 the log ratio of response rates is the dependent variable, the log ratio of reinforcement rates is the independent variable, the *a* parameter is the slope of the function, and log *b* is the *y*-intercept.

The *a* and log *b* parameters are derived from linear regression fits to the data. If *a* equals 1.0, the organism is perfectly matching. Values of *a* greater than 1.0 are indicative of overmatching, and values less than 1.0 indicate undermatching. Undermatching refers to a preference that is closer to indifference between the alternatives than predicted based

on relative reinforcement rate, whereas overmatching refers to allocation of behavior that is more extreme than expected based on the relative rates of reinforcement delivered by each response alternative (Baum, 1974; see McDowell, 1989, for discussion). Typically, subjects tend to undermatch the allocation of their behavior. The average sensitivity to relative rates of reinforcement in choice studies has been $a = 0.8$ (Baum, 1979; see Davison & McCarthy, 1988, for review). The other systematic deviation from strict matching is bias for one response alternative that is not accounted for by variations in relative reinforcement rate. Values of log b equal to 0 indicate no bias towards either alternative. The sign of log b indicates the direction of the bias (i.e., positive log b indicates bias towards the alternative on the numerator, whereas negative log b indicates bias towards the alternative on the denominator).

The generalized matching law is a widely accepted quantitative account of choice behavior and many studies have been conducted in order to test its generality (see Baum, 1979; Davison & McCarthy, 1988; Wearden & Burgess, 1982; Williams, 1988, for reviews). Applications of the generalized matching law have proven useful in understanding a variety of human behaviors (e.g., Borrero & Vollmer, 2002; Conger & Killeen, 1974; Murphy, Correia, Colby, & Vuchinich, 2005; Schroeder & Holland, 1969; Symons, Hoch, Dahl, & McComas, 2003; Vollmer & Bourret, 2000; see Fisher & Mazur, 1997, for review). For instance, Borrero and Vollmer used a matching law analysis to describe the relation between problem behavior of individuals with severe developmental disabilities and reinforcers maintaining these behaviors. The identification of the relation between reinforcers and the occurrence of problem behaviors could aid primary care

providers in understanding the conditions under which the behavior occurs and developing effective treatments for the reduction or elimination of problem behaviors. Similarly, the applications of the generalized matching law to drug-maintained behavior may provide useful information about the reinforcing efficacy of drugs. For instance, the bias parameter may provide a quantitative index of the relative reinforcing efficacy of drugs.

Applications of the Generalized Matching Law to Drug-Maintained Behavior

Recently, there has been greater interest in the application of the matching law to choice behavior maintained by drug reinforcers (e.g., Anderson, Velkey, & Woolverton, 2002; Anderson & Woolverton, 2000; Meisch & Spiga, 1998; Spiga, Maxwell, Meisch, & Grabowski, 2005; Woolverton, 1996; Woolverton & Alling, 1999; Woolverton & Anderson, 2006). Some laboratory studies have shown that the matching law adequately captures the relationship between relative response rates and relative rates of drug reinforcement. Table 1-1 summarizes findings of studies applying the generalized matching law to drug-maintained behavior on concurrent schedules of reinforcement. These studies were selected based on the following criteria: use of concurrent schedules of reinforcement, drug as reinforcer, and generalized matching law analysis provided or the inclusion of sufficient data to derive such an analysis. Across studies, the generalized matching law adequately accounted for behavior maintained by drugs ($r^2 = 0.83$), subjects tended to undermatch ($a = 0.88$), and bias estimates were negligible ($\log b < 0.25$).

Table 1-1

Studies Using the Generalized Matching Law to Account for the Allocation of Behavior Between Alternative Sources of Drug Reinforcement[a]

Study	Drug	Dose (mg/kg)	Species	Schedule of reinforcement	*a*	log *b*	r^2
Iglauer & Woods (1974)[b]	Cocaine	0.013 - 0.8	Monkeys	Conc VI VI	2.41	-0.16	0.88
Llewellyn, Iglauer, & Woods (1976)[b]	Cocaine	0.013 - 0.8	Monkeys	Conc VI VI	0.85	-0.07	0.75
Woolverton (1996)	Cocaine	0.025	Monkeys	Conc VI VI	0.63	-0.05	0.79
		0.500		Conc VI VI	0.70	0.24	0.76
		1.000		Conc VI VI	0.62	0.25	0.73
Meisch & Spiga (1998)	Pentobarbital	1.0-4.0	Monkeys	Conc VR 16 VR 16	1.39	0.02	0.98
		1.0-4.0		Conc VR 32 VR 32	1.42	0.03	0.98
		1.0-4.0		Conc VR 64 VR 64	1.13	0.05	0.86
Anderson & Woolverton (2000)	Alfentanil	0.001	Monkeys	Conc VI VI	0.61	0.01	0.93
		0.004		Conc VI VI	0.40	-0.07	0.79
	Methohexital	0.250		Conc VI VI	0.66	-0.01	0.85
		0.500		Conc VI VI	0.60	0.01	0.84
	Cocaine	0.500		Conc VI VI	0.57	-0.01	0.91
Martinetti et al. (2000)	Ethanol	2, 5, and 10% (vol/vol)	Rats	two-bottle limited-access paradigm	0.71	0.07	0.44
Anderson, Velkey, & Woolverton (2002)	Cocaine	0.025	Monkeys	Conc VI VI	0.63	-0.15	0.80
		0.050		Conc VI VI	0.55	-0.13	0.67
Martinetti, Khan, & Lewis (2007)	Ethanol	2, 4, 6, and 10% (vol/vol)	Rats	two-bottle limited-access paradigm	1.36	0.33	0.48

[a]Estimates of sensitivity (a), bias (log b) and variance accounted for by the model (r^2) presented are based on the average of individual subjects' matching-law fits in each study. Studies are listed in chronological order.

[b]Matching law parameters were derived from a reanalysis of the data presented in the publication.

Iglauer and Woods (1974) were the first to demonstrate the usefulness of concurrent VI VI schedules for the study of the reinforcing efficacy of drugs. In this study, monkeys were trained to respond on a concurrent schedule of reinforcement for cocaine infusions. Responses on one lever were reinforced by a constant dose (0.05 or 0.1 mg/kg/infusion), whereas responses on the other lever were reinforced by a variable dose (0.013-0.8 mg/kg/infusion). As the magnitude of the reinforcer was varied across conditions, monkeys allocated more behavior to the lever delivering the higher dose.

More recently, Woolverton and colleagues have investigated the applicability of the generalized matching law to cocaine-maintained behavior in concurrent VI VI schedules (Anderson et al., 2002; Anderson & Woolverton, 2000; Woolverton, 1996; Woolverton & Alling, 1999; Woolverton & Anderson, 2006). In the first study of this series, Woolverton trained monkeys to respond for cocaine infusions on concurrent VI VI schedules of reinforcement. The VI schedules were varied to provide a range of reinforcement-rate ratios across conditions. There was a tendency toward undermatching ($a \approx 0.76$), that is, for response allocation to be less extreme than expected based on the reinforcement rates delivered for each alternative. As stated previously, however, undermatching tends to be the typical finding with food-maintained behavior (see Baum, 1979; Davison & McCarthy, 1988; Wearden & Burgess, 1982, for reviews). Overall, the monkeys' allocation of behavior in the Woolverton study was well described by the generalized matching law (see Table 1-1).

Applications of the Generalized Matching Law to Alcohol-Maintained Behavior

Currently, approximately 9% of American adults abuse alcohol or are alcohol-dependent, causing enormous social and health concerns (National Institute on Alcohol Abuse and Alcoholism [NIAAA], June, 2004). The study of alcohol self-administration in nonhumans has shown to be a useful tool for understanding human alcohol abuse and dependence (see Meisch, 1977, for review). In addition, Vuchinich and Tucker (1988) proposed that behavioral theories of choice could provide a useful framework for understanding behavior maintained by alcohol and the effect of changes in alcohol availability on choice.

Martinetti, Andrzejewski, Hineline, and Lewis (2000) conducted the first study using a matching-law analysis of alcohol self-administration in a choice procedure. Rats were trained to drink alcohol solutions from two concurrently available graduated drinking tubes during 1-h sessions. Rats were divided into seven groups that experienced the choice conditions in different orders. Choice conditions were consecutive sessions in which rats experienced every possible pairwise combination of 0, 2, 5, and 10% alcohol solutions. The volume of solution consumed was used as the dependent measure. To analyze the results, Martinetti and colleagues used a modified version of the generalized matching law:

$$\log\left(\frac{V_1}{V_2}\right) = a\log\left(\frac{C_1}{C_2}\right) + \log b, \tag{3}$$

where V refers to the consumed volume of solution, C refers to the alcohol concentration, and the subscripts refer to the alternatives. For 16 of the 28 rats, the generalized matching

law equation accounted for approximately half the variance in the data ($r^2 \geq 0.45$). For the remaining 12 rats, the generalized matching law equation did not capture the data adequately (e.g., $r^2 < 0.01$, for 2 rats, negative slopes). Compared to results obtained with food-maintained behavior and behavior maintained by other drugs (see Table 1-1), the volume of alcohol consumed in the Martinetti and colleagues study was not well described by the generalized matching law. A more recent study by Martinetti, Kahn, and Lewis (2007) found similar results with different rat strains.

It is not entirely clear why the generalized matching law equation did not adequately describe the data from the Martinetti and colleagues (2000, 2007) studies. The most apparent feature of these studies that may account for the results is that Martinetti and colleagues did not use a free-operant procedure typical of choice studies, in which experimental subjects allocate their behavior on two concurrently available VI schedules of reinforcement. The use of volume consumed instead of absolute g/kg of alcohol as the dependent measure also is problematic because, at high concentrations, less volume is required to reach the same g/kg consumed. Thus, it is difficult to directly compare the derived parameters of sensitivity and bias from the Martinetti and colleagues studies to those obtained with other reinforcers under typical concurrent VI VI schedules. A study using the typical free-operant choice procedure is needed to determine the adequacy of the generalized matching law for describing choice behavior maintained by alcohol. Experiment 1 (see Chapter 2) extended the Martinetti and colleagues (2000) study with a free-operant concurrent VI VI procedure.

Choice and Conditioned Reinforcement

Choice behavior is mediated by environmental variables such as delay to reinforcement or the presence of stimuli signaling reinforcer availability (see Davison & McCarthy, 1988, for review). Extensions of the generalized matching law have been developed to include the impact of environmental stimuli on choice behavior (e.g., Davison, 1987; Wardlaw & Davison, 1974). Stimuli that signal the availability of reinforcement become conditioned reinforcers. Conditioned reinforcers can be defined as initially neutral stimuli that acquire the ability to maintain responding (i.e., reinforcing value) as a result of Pavlovian association with a primary reinforcer (see Rescorla & Solomon, 1967; see Fantino, 1977; Hendry, 1969; Williams, 1994, for reviews).

Hull (1943) was probably the first to state that stimuli that are temporally contiguous to primary reinforcers become conditioned reinforcers. Hendry (1969) refers to Hull's statement as the S-S hypothesis, in contrast to the S-R or discriminative-stimulus hypothesis proposed by Skinner (1938; see also Keller & Schoenfeld, 1950). The S-R hypothesis states that for a stimulus to become a conditioned reinforcer, a reinforced response must occur in the presence of the stimulus. Thus, only a discriminative stimulus may become a conditioned reinforcer. As Hendry points out, however, both of these hypotheses have their limitations and alternative hypotheses have been proposed (e.g., information hypothesis; Egger & Miller, 1962, 1963). Much research has been devoted to further understanding the underlying mechanism(s) through which conditioned reinforcement affect(s) behavior (see Hendry, 1969, for review). With the advent of methods for the study of drug-maintained behavior and the increased

interest in the impact of conditioned reinforcement on operant behavior, study of the role of conditioned reinforcers in the maintenance of drug seeking and taking has become more prevalent.

Drug-Associated Cues

Consistent with classic theories of learning (Hull, 1943; Keller & Schoenfeld, 1950; Mowrer, 1960; Skinner, 1938), drug-associated cues can function as conditioned reinforcers, as a result of being associated with a drug that serves as primary reinforcer (e.g., Di Ciano & Everitt, 2004; Hogarth, Dickinson, & Duka, 2003; Schuster & Woods, 1968). For instance, Smith, Werner, and Davis (1977) showed that, after five 10-h sessions, a neutral auditory stimulus paired with alcohol acquired conditioned reinforcing properties, as indicated by its ability to maintain responding in the absence of alcohol deliveries. Current theories of drug addiction include drug-associated cues as a key factor in the maintenance and persistence of drug-taking behavior (e.g., Everitt & Robbins, 2005; Robinson & Berridge, 1993, 2000). According to Robinson and Berridge's incentive-sensitization theory of addiction, drugs of abuse enhance the activation of the mesotelencephalic dopamine system that, in turn, attributes incentive properties (i.e., value) to cues associated with the activation of the dopamine system (i.e., drug-associated cues). With repeated drug use, the neural system adapts and becomes sensitized to drug-associated cues, making them highly desirable. Because sensitization of the dopamine system is related to learning processes, the incentive properties of the cues become associated with drug-taking behavior. Thus, being in the presence of drug-associated cues

activates neural processes that drive excessive drug-taking behavior (see also Bindra, 1969, 1974, for related discussions).

Others also have suggested that stimuli that accompany the delivery or consumption of drugs are closely related to compulsive drug use (Di Chiara, 1999; Stewart, de Wit, & Eikelboom, 1984). Moreover, the acquired value of the drug-associated cues selectively controls drug seeking and drug taking (e.g., Baxter & Hinson, 2001; Field, Mogg, & Bradley, 2005a; Field, Mogg, Zetteler, & Bradley, 2004; Gross, Jarvik, & Rosenblatt, 1993; Sayette & Hufford, 1994; Waters & Feyerabend, 2000) and has been closely related to drug craving (Field, Mogg, & Bradley, 2005b) and relapse (Stewart et al.) in both animals and humans. Recently, biases for drug-associated cues also have been shown to predict drug relapse in abstinent individuals three months after treatment for heroin addiction (Marissen et al., 2006).

Carter and Tiffany (1999) conducted a meta-analysis of cue-reactivity research with humans addicted to various drugs and found strong support for the role of drug-associated cues in self-reported ratings of craving. In cue-reactivity studies, participants typically are presented with drug-associated stimuli (e.g., paraphernalia, environments) and measurements of craving or desire to use drugs are recorded with self-reports and/or physiological responses. Carter and Tiffany found that across all studies analyzed with participants addicted to various drugs, drug-associated cues triggered craving and desire to consume drugs. This finding emphasizes the need to consider role of the context on drug-maintained behavior. Context can be defined as any environmental factor that determines behavior and impacts the degree of conditioning (Fantino, 2001). A context

can be anything from a stimulus paired with delivery of reinforcement (i.e., conditioned reinforcer) to delay to primary reinforcement to the availability of other sources of reinforcement. Carter and Tiffany noted that future research should focus on investigating the variables that modulate context effects on behavior. Given the important role that drug-associated cues play in the maintenance of drug taking, craving, and relapse, identifying the underlying processes through which they exert their actions is critical to understanding and treating drug abuse and dependence.

Methods for the Study of Drug-Associated Cues

Several procedures have been used to study the role of drug-associated cues or conditioned reinforcers in the maintenance of drug taking. One such method is the *new-response procedure*. In this procedure, a purported conditioned reinforcer is used to reinforce the acquisition of a novel response (Williams, 1994; see Di Ciano & Everitt, 2004, for application to drug-associated cues; see Davis & Smith, 1987, for review). Di Ciano and Everitt assessed the conditioned reinforcing properties of drug-associated cues by training rats to respond in order to obtain presentation of a stimulus that had been previously paired with a drug. They found that the stimulus previously paired with cocaine and heroin consistently maintained a new response over several sessions, without the presentation of the drugs. The fact that rats continued to respond for the presentation of the drug-associated stimulus provides support to the idea that these stimuli acquire reinforcing properties of their own as a result of the drug-stimulus pairings (i.e., Pavlovian conditioned stimulus-unconditioned stimulus association). However, the new-response procedure has several limitations. First, stimulus change alone could produce

increases in responding (see Stubbs, 1971; Williams, 1994), rendering the conditioned reinforcement interpretation unnecessary unless appropriate control groups are used. Second, and most importantly, the effect under study has a relatively short duration. The short duration of the effect has been interpreted as extinction of the conditioned value of the conditioned reinforcer.

Another common procedure for the study of drug-associated cues is *resistance to extinction*, in which responding in the presence or absence of a purported conditioned reinforcer is evaluated under extinction of primary reinforcement (see Bugelski, 1938; Kimble, 1961, for review). A stimulus is said to be a conditioned reinforcer if its presentation produces greater persistence of responding during extinction conditions compared to when the stimulus is absent under similar conditions. Bugelski trained rats to retrieve food from a food receptacle in an operant chamber. During training, each food presentation was accompanied by a click. In a subsequent condition, a lever was inserted into the operant chamber and lever presses resulted in presentation of the food and the click. Next, lever pressing was extinguished by eliminating food presentations. For half the rats, the click was presented contingent on lever presses (click-extinction group). For the other rats, lever presses had no programmed consequences (extinction group). Bugelski found that the response-dependent presentation of the click during extinction resulted in greater persistence of behavior. These results can be interpreted as the click functioning as a conditioned reinforcer due to its previous association with food.

Results obtained using this procedure cannot be interpreted unequivocally, however, because the degree of stimulus change could also account for results (i.e.,

generalization decrement; Williams, 1994). For instance, in the Bugelski (1938) experiment one could argue that the extinction contingency was more easily discriminable for the rats in the extinction group (i.e., no click presented contingent on responding), because the degree of stimulus change between conditions was greater. Thus, lever pressing is more resistant to extinction in the click-extinction group not necessarily because the click functions as a conditioned reinforcer, but because the rats cannot as easily discriminate that the conditions have changed. Additionally, as with the new-response procedure, the conditioned reinforcement effects are transient.

Second-order schedules were devised to circumvent the problem of brevity of the conditioned reinforcement effect associated with the resistance to extinction and new-response procedures. In this procedure, the presentation of stimuli according to the requirements of a schedule of reinforcement maintains a higher-order pattern of responding controlled by another schedule of reinforcement, which controls delivery of the primary reinforcer (Kelleher, 1966). For example, the first response to occur after 1 min would produce a brief stimulus change (e.g., flash a light) and after this schedule requirement has been completed 20 times, the stimulus change would occur along with the primary reinforcer. Thus, the brief stimulus presentations are interpreted as conditioned reinforcers due to the fact that they maintain responding.

Second-order schedules have the benefit of maintaining high rates of responding with few presentations of primary reinforcement. In addition, second-order schedules allow for steady patterns of behavior to be studied for prolonged periods of time. Second-order schedules have been widely used to study drug-associated conditioned

reinforcement (see Katz & Goldberg, 1987; Schindler, Panlilio, & Goldberg, 2002, for reviews). As is the case with the new-response procedure, however, the stimulus change alone could account for increases in responding. Thus, the interpretation of the stimulus presentations as conditioned reinforcers cannot be made unequivocally.

Finally, another procedure widely used for the study of drug-associated cues is *conditioned place preference*. An interesting aspect of this procedure is that it allows for the study of choice for a drug-associated context. In this procedure, experimental subjects are exposed to different contextual cues (e.g., different experimental chambers) across trials in which either a drug or a saline injection is given by the experimenter. During a test trial, injections are withheld and the experimental subject is given the option to choose between the saline-associated context and the drug-associated context. The relative time spent in each context serves as the measure of preference. Overall, subjects tend to spend relatively more time in the context previously associated with the drug injection (see Bardo & Bevins, 2000, for review). Despite the usefulness of this procedure, it has some limitations. For instance, Bardo and Bevins noted that drug administration prior to exposure to a context may retard familiarization with the context, and as a result, novelty-seeking behavior during the test session in which no drug is administered may be a confounding variable. In addition, this procedure does not easily lend itself for a dose-effect analysis of drug effects typically conducted in the area of behavioral pharmacology. Another shortcoming of this procedure is that choice for a drug-associated context cannot be easily conceptualized within the framework of behavioral models of choice. In fact, none of the procedures described above typically are

used for quantitative analyses of behavior maintained by conditioned reinforcers. The standard procedure for such analysis and for which a well-established conceptual framework has been developed is the concurrent-chains procedure.

Concurrent-Chains Procedure

Within the field of operant learning, the concurrent-chains procedure is the most frequently used procedure for studying conditioned reinforcement. This procedure allows for a quantitative analysis of the determinants of the *value* of the conditioned reinforcer (Williams, 1994). Value can be understood as the efficacy of a stimulus to maintain operant responding (Mazur, 2001). Furthermore, the concurrent-chains procedure has all the advantages of choice procedures over single schedules described above (e.g., relative measure of behavior).

The concurrent-chains procedure, originally introduced by Autor (1969; see also Herrnstein, 1964), allows for the study of conditioned reinforcement by arranging a situation in which experimental subjects choose between two concurrently available alternatives (i.e., initial links) to obtain access to one of two mutually exclusive stimulus contexts that are paired with primary reinforcement (i.e., terminal links). Access to the terminal-link stimulus context functions as a conditioned reinforcer (e.g., Moore, 1985; Dunn, Williams, & Royalty, 1987; see Williams, 1994) and relative allocation of behavior during the initial links is a measure of the value of the terminal-link stimulus context.

Figure 1-1 shows a diagram of a concurrent-chains procedure. During the initial

links, two concurrently available response alternatives provide access on VI schedules of reinforcement to mutually exclusive terminal links. Once the VI schedule on one of the initial-link alternatives times out and a response has been emitted, initial-link stimuli are turned off and the corresponding terminal-link stimulus is presented. The primary reinforcer (e.g., food) is delivered for responding during the terminal link once the fixed-interval (FI) schedule has timed out. After the primary reinforcer is delivered, terminal-link stimuli are extinguished and the initial links are presented again.

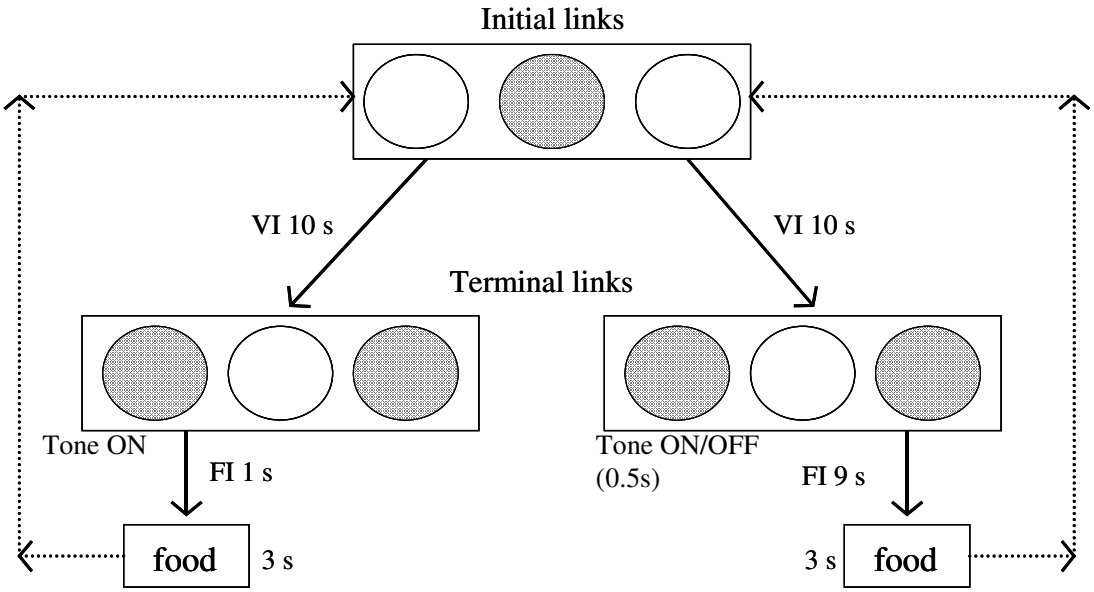

Figure 1-1. Diagram of a concurrent-chains schedule. In the initial links, both side manipulanda are lit and the center manipulandum is dark. Responding on the side manipulanda occasionally produces entry into one of the mutually exclusive terminal links signaled by the steady or pulsing tone (on and off every 0.5 s). During the terminal links the side manipulanda are dark and the center manipulandum is lit. Responding in the terminal links is occasionally reinforced with food. Following end of the terminal links, the initial links are re-presented.

Herrnstein (1964) found that the relative allocation of responding during the initial links roughly matched the relative rates of reinforcement delivered in the terminal links. Thus, Herrnstein proposed that the matching law could be directly applied to performance on concurrent chains. Fantino (1969) challenged this suggestion when he found that changes in schedule parameters (e.g., initial-link schedules) limited the applicability of the matching law to concurrent-chains performance. To account for these limitations of the matching law, several quantitative models of choice between two conditioned reinforcers have been developed (see Mazur, 2001; Mazur, 2006, for reviews). The most widely used and tested models will be briefly described.

Delay-Reduction Theory

Developed by Fantino (1969; Squires & Fantino, 1971), delay-reduction theory (DRT) is the most influential quantitative model of concurrent-chains performance. The basic premise of DRT is that the terminal-link stimuli are conditioned reinforcers because they signal a reduction in time to primary reinforcement relative to the average time to reinforcement in the absence of differential stimuli (see Gibbon & Balsam, 1981, for a related theory of classical conditioning). In quantitative terms,

$$\frac{B_1}{B_2} = \left(\frac{R_1}{R_2}\right)\left(\frac{T_{total} - T_{t1}}{T_{total} - T_{t2}}\right), \tag{4}$$

where B represents initial-link responses rates, R represents overall rates of primary reinforcement, the subscripts refer to the response alternatives, T_{total} is the mean time to primary reinforcement from the beginning of the initial links, and T_{t1} and T_{t2} are the mean times to primary reinforcement from the beginning of the terminal links (Squires &

Fantino, 1971). According to DRT, choice depends on the absolute duration of the initial links relative to the duration of the terminal links. In other words, conditioned-reinforcer value is determined by the overall temporal context. It is important to note the relation between DRT and the matching law. If one removes the rightmost expression of Equation 4, as would be the case if terminal-link schedules were zero, Equation 4 is reduced to the strict matching law (Equation 1).

Another class of quantitative models for responding on concurrent chains is based on the concatenated matching law (Baum & Rachlin, 1969). The concatenated matching law is an extension of the generalized matching law (Equation 2) that includes additional independent variables that can impact the relative allocation of behavior in a choice situation (e.g., magnitude of reinforcement, delay to reinforcement). For instance, Equation 5 represents a version of the concatenated matching law that includes the impact of relative *rates* of reinforcement (R_1/R_2) and the ratio of any other potential reinforcement variable that may affect responding (X_1/X_2) on the relative allocation of behavior (B_1/B_2),

$$\log\left(\frac{B_1}{B_2}\right) = a_R \log\left(\frac{R_1}{R_2}\right) + a_X \log\left(\frac{X_1}{X_2}\right) + \log b\,. \tag{5}$$

Davison (1983) suggested that concurrent schedules could be conceived as a concurrent chain with a 0-s terminal link. Consequently, the concatenated matching law could be extended to concurrent-chains schedules. One ratio of variables (i.e., R_1/R_2) represents terminal-link entry rate (i.e., presentation of conditioned reinforcers) and a concatenated ratio (i.e., X_1/X_2) represents delivery of the primary reinforcement in the

presence of the terminal-link stimulus context, each with its corresponding sensitivity parameter (a_R and a_X, respectively). Thus, quantitative models of behavior on concurrent chains based on the concatenated matching law include both the role of conditioned reinforcement rate and primary reinforcement rate on response allocation in the initial links. This idea has been extended and formalized by other researchers (e.g., Grace, 1994; Mazur, 2001).

Contextual-Choice Model

Grace (1994) proposed the contextual-choice model (CCM) as a new model of concurrent-chains performance based on the generalized matching law. Grace includes terms that capture both initial-link and terminal-link reinforcement rates as determinants of choice responses during the initial link. Expressed quantitatively,

$$\frac{B_1}{B_2} = b\left(\frac{R_{i1}}{R_{i2}}\right)^{a_i}\left(\frac{R_{t1}}{R_{t2}}\right)^{a_t(T_t/T_i)}, \tag{6}$$

where B represents initial-link responses per min, R_i represents terminal-link entry rates (i.e., rate of conditioned reinforcement), R_t represents rate of primary reinforcement in the terminal links, and the subscripts refer to the response alternatives. The free parameters a_i and a_t represent sensitivity to relative reinforcement rates in the initial and terminal links, respectively. The b parameter represents bias (as in the generalized matching law, Equation 2). T_i is the average initial-link duration and T_t is the average terminal-link duration. The ratio T_t/T_i represents the main assumption of CCM that sensitivity to relative rates of reinforcement in the terminal links (i.e., value of conditioned reinforcers) changes as a function of the overall time to reinforcement (i.e.,

the temporal context). Note that, if the rightmost expression of Equation 6 is removed, as would be the case with 0-s terminal links, the equation reduces to the generalized matching law (Equation 2).

Although the concurrent-chains models described above have different assumptions of the determinants of choice, they make similar basic predictions about choice in concurrent chains. Differences in specific predictions of quantitative models of concurrent-chains performance have been reviewed previously (see Mazur, 2001). A comparison of these models will not be addressed in the present document because the differences between the models are beyond the scope of the present studies. Instead, the main focus is to evaluate the overall adequacy of quantitative models of concurrent-chains choice and conditioned reinforcement in general, in accounting for alcohol-maintained behavior. Therefore, as an initial step, a prediction common to all models will be tested.

Initial-Link Effect

One basic prediction shared by the models of concurrent-chains performance presented above has been termed the *initial-link effect*. The initial-link effect is demonstrated when, given unequal terminal links (e.g., FI 1-s vs. FI 9-s controlling primary reinforcement delivery), preference for the higher reinforcement terminal link is made less extreme by increasing the length of the initial-link schedules (Fantino, 1969). According to DRT, the decrease in preference is reflective of the decrease in the relative value of the conditioned reinforcers. From a CCM perspective, the decrease in preference is due to a change in sensitivity to relative rates of reinforcement in the terminal links.

Nonetheless, the general predictions for the initial-link effect are the same (i.e., less extreme preference). The predictions of the models will be explained through an example. If initial links are VI 10 s, the left terminal link delivers primary reinforcers on a FI 1-s schedule, and the right terminal link delivers primary reinforcers on a FI 9-s schedule, both models predict preference for the left initial link.

The specific prediction for DRT is derived from Equation 4 in the following way. First, the average times to primary reinforcement are 11 s and 19 s on the left and right terminal links, respectively. R_1 represents the rate of primary reinforcement on the left terminal link, $R_1 = (60/11) = 5.45$ reinforcers/min, and R_2 represents the rate of primary reinforcement on the right terminal link, $R_2 = (60/19) = 3.15$ reinforcers/min. The ratio of R_1 and R_2 results in the left-most expression of Equation 4, $R_1/ R_2 = 1.73$. Then, the right-most expression of Equation 4 is derived. T_{total} consists of average time in the initial links plus average time in the terminal links. In this case, the average time in the initial links is 5 s and the average time to primary reinforcer after entering the terminal links is 5 s. Because both initial links are concurrently available and are independent, T_{total} is 10 s. Upon entering the left terminal link, the delay to primary reinforcer is $(T_{total} - T_{tL})$, or 10-s – 1-s = 9-s closer than it had been at the beginning of the initial link. Conversely, upon entering the right terminal link, the primary reinforcer is only 10-s – 9-s = 1-s closer. The right-most expression, $(T_{total} - T_{tL}) / (T_{total} - T_{tR})$, results in (9/1) = 9. Finally, according to Equation 4, the product of the two ratios previously calculated [i.e., (R_1/ R_2) and $(T_{total} - T_{tL}) / (T_{total} - T_{tR})$] provides an estimate of the preference ratio, which in this case is (1.73 * 9) = 15.57. Thus, preference for the left terminal link, as measured by the

ratio of responses on the initial links, will be approximately 15 times greater than for the right terminal link.

When both initial links are increased to VI 60-s schedules, the rightmost component of Equation 4 is changed because the average time to reinforcement (T_{total}) is increased. Now T_{total} equals 35-s and delay reduction to primary reinforcer on the left and right will equal 33-s and 26-s, respectively. Entering the left terminal link now signals a relatively smaller reduction in overall time to reinforcement compared to the right terminal link. As a result, DRT now predicts that behavior allocated to the left initial link should only be 2.2 times greater than behavior allocated to the right. Thus, the initial-link effect is due to a decrease in the relative value of the conditioned reinforcer, as determined by the rightmost component of Equation 4.

In the case of CCM, however, the initial-link effect is due to a change in the relative temporal context in which the primary reinforcer is delivered (i.e., the T_t/T_i exponent of the right-most component of Equation 5). In other words, if the initial links are increased from a VI 10-s to a VI 60-s, the T_t/T_i ratio would change from 1 to 0.17, decreasing sensitivity to relative value of the conditioned reinforcer which is directly determined by relative rates of reinforcement in the terminal links. As a result of this change, Equation 6 predicts that the almost six-fold difference in preference when the initial links are VI 10-s schedules will decrease to approximately 1.34 when the length of the initial links is increased to VI 60 s. If the primary reinforcer is a drug, the initial-link effect could be interpreted as a decrease in the sensitivity to the relative value of a more potent drug-associated context as a result of an environmental manipulation. If one

considers the role of drug-associated cues in drug craving and relapse, extension of this effect to drug-maintained behavior becomes relevant for understanding how to modulate the value of drug-associated stimuli that evoke craving and relapse.

Use of the Concurrent-Chains Procedure for the Study of Drug-Associated Cues

Although procedures similar to standard concurrent chains have been used to study impulsivity with drug reinforcers (e.g., Perry, Nelson, Anderson, Morgan, & Carroll, 2007; Woolverton, Myerson, & Green, 2007), the use of manipulations aimed at decreasing choice for a preferred drug-associated context have not been studied. Further, the only report of a standard concurrent-chains procedure with drug reinforcers comes from Iglauer and Woods (1974). Iglauer and Woods used the concurrent-chains procedure with a cocaine reinforcer to separate the disruptive effect of the drug from the choice responses. However, the use of fixed-ratio schedules of reinforcement in the terminal links of their experiment precludes quantitative analyses of these data because reinforcement rate is confounded with response rate. An additional factor that precludes a quantitative analysis is that the models described above are based on time to reinforcement, and these data were not provided in the original Iglauer and Woods study and cannot be derived due to the use of ratio schedules. Thus far, quantitative models of concurrent-chains performance have not been extended to choice between two contexts associated with drug reinforcement.

Summary

Models of concurrent-chains performance are based on the matching law. As stated earlier, however, the applicability of the generalized matching law to alcohol-maintained behavior remains to be corroborated. Therefore, Experiment 1 (see Chapter 2) was conducted to determine the adequacy of the generalized matching law in accounting for choice behavior maintained by alcohol. The purpose of Experiment 2 (see Chapter 3) was to extend the use of the concurrent-chains procedures to the study of choice between contexts associated with different rates of alcohol reinforcement. Experiment 3 (see Chapter 3) aimed at demonstrating the initial-link effect with choice behavior maintained by alcohol. Such finding may serve as an initial step toward a quantitative account of choice between two contexts differentially associated with drug reinforcement and may provide a useful animal model to assess behavioral treatments aimed at decreasing alcohol seeking, craving, and relapse.

CHAPTER 2

MATCHING LAW ANALYSIS OF RATS' ALCOHOL SELF-ADMINISTRATION IN A FREE-OPERANT CHOICE PROCEDURE[1]

Abstract

The generalized matching law quantitatively describes the relation between relative response allocation and relative reinforcement allocation in a choice situation and has accounted well for drug-maintained choice behavior. Previous studies applying the generalized matching law to alcohol-maintained choice, however, have produced somewhat atypical findings (e.g., low variance accounted for, negative sensitivity values). These findings may be the result of the procedures used in the previous alcohol studies (e.g., two-bottle choice procedure, volume consumed as dependent variable). In the present study, a free-operant choice procedure using concurrent variable-interval schedules of alcohol reinforcement was used. Across conditions, rates of alcohol deliveries produced by two response alternatives were varied to assess the adequacy of the generalized matching law in accounting for alcohol-maintained choice. Results showed that the generalized matching law provided a good description of changes in the relative allocation of behavior with changes in the relative rate of alcohol delivery. Thus, the generalized matching law may serve as a useful tool in the study of alcohol-related choice. Although choice procedures have been used in assessing therapies for alcohol

[1] Co-authored by Corina Jimenez-Gomez and Timothy A. Shahan.

abuse, future studies could benefit from the quantification provided by the bias and sensitivity parameters of the generalized matching law.

Introduction

Choice procedures have been used to study the relative reinforcing efficacy of different drugs, different doses of the same drug, or drug versus nondrug reinforcers (e.g., Iglauer & Woods 1974; Llewelyn, Iglauer, & Woods, 1976; Woolverton, 1996; see Bergman & Paronis, 2006, for review). In these procedures, responding on two concurrently available options is reinforced according to independently arranged schedules of reinforcement. Relative reinforcing efficacy of the two reinforcers is measured by the relative allocation of behavior to the two response options (Williams, 1988).

Vuchinich and Tucker (1988) proposed that behavioral theories of choice could provide a useful framework for understanding alcohol abuse. One such theory of choice is the generalized matching law (Baum, 1974), which states that the relative allocation of behavior to two options is a power function of the relative allocation of reinforcement obtained at the two options. Quantitatively that is:

$$\log\left(\frac{B_1}{B_2}\right) = a\log\left(\frac{R_1}{R_2}\right) + \log b\,, \qquad (1)$$

where B represents responses rates, R represents reinforcement rates, and the subscripts refer to two response options. The a parameter is the slope of the function and refers to

sensitivity of relative response rates to variations in relative rates of reinforcement, and log *b* is the *y*-intercept and refers to *bias* for one option unrelated to changes in relative reinforcement rates.

The generalized matching law previously has been used to account for the allocation of behavior maintained by drug reinforcers in choice procedures (e.g., Anderson et al., 2002; Anderson & Woolverton, 2000; Woolverton, 1996; Woolverton & Alling, 1999; see Dallery & Soto, 2004, for review of applications of Herrnstein's hyperbola [Herrnstein, 1970]). The generalized matching law has provided a good description of the relationship between relative response rates and relative rates of drug reinforcement delivered according to concurrent variable-interval (VI) schedules, accounting for 60-99% of the variance in the data. With both food- (see Baum, 1979; Wearden & Burgess, 1982, for reviews) and drug-maintained behavior (e.g., Anderson & Woolverton, 2000; Iglauer & Woods, 1974), sensitivity values have been reported to be around 0.8.

Martinetti and colleagues (2000) reported the first study applying the generalized matching law to alcohol consumption in a choice situation. Rats were trained to drink solutions of different alcohol concentrations across conditions in a two-bottle choice procedure. Unlike results obtained with other drug- or food-maintained behavior, the allocation of responding (measured as relative volume consumed) was not well described by the generalized matching law, and the average variance accounted for was lower (r^2 = 0.44) than typically obtained with other drugs ($r^2 \approx 0.8$). In addition, for a quarter of the rats, sensitivity values were negative or lower than 0.2 (see Martinetti et al., 2007, for

similar results). Finally, the use of volume consumed instead of absolute g/kg of alcohol as the dependent measure is problematic because, at high concentrations, less volume is required to reach the same g/kg consumed. Thus, it is unclear whether the poor fits of the generalized matching law in the Martinetti and colleagues (2000) study resulted from the procedures used or the use of alcohol as the reinforcer. Therefore, a study using a more typical procedure with concurrent VI schedules and changes in relative rates of alcohol delivery across conditions is needed to further assess the applicability of the generalized matching law to alcohol-maintained choice behavior.

Method

Subjects

Six experimentally naïve male Long Evans rats were used. The rats were approximately 120 days old at the beginning of the experiment and were maintained at 80% of their free-feeding weights (i.e., 320-350 g) by supplementary feeding of rat chow after the daily sessions. The rats were housed individually in a temperature-controlled colony with a 12:12 hr light/dark cycle (lights on at 7:00 a.m.). Experimental sessions were conducted 7 days per week during the light periods at approximately the same time every day. Water was freely available in the home cage. Animal care and housing was conducted in accordance to the standards set by the Guide for the Care and Use of Laboratory Animals (National Research Council, 1996).

Apparatus

Four Med Associates® operant conditioning chambers were used. Each chamber was approximately 30 cm long, 24 cm wide, and 21 cm high, and housed in a sound-attenuating cubicle. The back panel of each chamber was equipped with five nose pokes. Each nose poke hole was 2.5 cm square and 2.2 cm deep. An infrared detector was located across each nose poke unit 1.0 cm from the front. A yellow 6.4 mm diameter stimulus light was mounted flush behind the back wall of each nose poke. Each chamber contained a 28-V DC houselight at the top center of the front panel and a solenoid-operated dipper that delivered the liquid solutions. Extraneous noise was masked by a chamber ventilation fan and white noise. Control of experimental events and data recording was conducted using Med Associates® interfacing and programming. Solutions were prepared with distilled water, table sugar, and 95% stock ethanol.

Procedures

Training. A modified sucrose-fading procedure (see Samson, 1986) as described by Shahan (2002) was used. During the first session, rats were trained to respond on two nose pokes using an autoshaping procedure (Brown & Jenkins, 1968) and a 10% sucrose 2% alcohol solution as the reinforcer. Across sessions, the alcohol concentration was increased while the sucrose was faded until reaching 0% sucrose 10% alcohol. At the same time, the response requirement gradually was increased and responding was placed on a random-ratio (RR) schedule. Once responding under an RR15 had stabilized, concurrent VI 30-s VI 30-s schedules of reinforcement (Fleshler & Hoffman, 1962) were introduced. All sessions ended after 30 min.

Concurrent schedules. For all rats, the schedule of reinforcement for both alternatives was gradually increased across approximately 10 sessions to VI 60 s for the first condition. A 0.5-s change-over-delay (COD) was imposed for switching from one option to the other and was timed from the first response on the changed-to alternative. The overall arranged rate of alcohol deliveries (i.e., summed across the two alternatives) remained constant across conditions but the ratio of alcohol deliveries provided by the two options varied as follows: 1:1 (VI 60s VI 60s), 3:1 (VI 40s VI 120s), 9:1 (VI 33.33s VI 300s), 1:3 (VI 120s VI 40s), and 1:9 (VI 300s VI 33.33s). The order in which rats were exposed to these conditions was counterbalanced. All conditions lasted 20 sessions (e.g., Weatherly, Grove, & Beste, 2007).

Results

As expected, repeated-measures ANOVA of total obtained dipper deliveries across the two options showed no significant effect of condition, $F(4, 20) = 2.408$, $p = .08$, suggesting that overall alcohol delivery rate was maintained constant throughout the experiment. Accordingly, total g/kg of alcohol delivered per session also did not differ significantly across conditions, $F(4, 20) = 2.265$, $p = .098$, Mean = 0.67 g/Kg. Figure 2-1 shows average response rates for the two options across the last 5 sessions of each condition plotted as a function of the log ratio of scheduled alcohol deliveries in each condition. For all rats, response rates were higher on the alternative providing the higher alcohol delivery rate. Repeated-measures ANOVA showed a significant condition by option interaction, $F(4, 20) = 12.89$, $p < .001$.

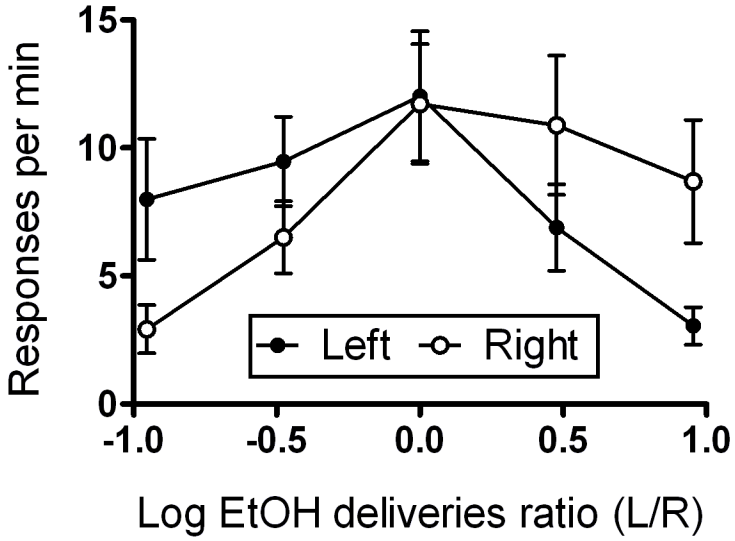

Figure 2-1. Response rates as a function of log ratios of scheduled alcohol deliveries (left/right). Closed and open data points represent response rates on the left and right response alternatives, respectively. Each data point represents the average of the last 5 sessions of each condition for all rats. Error bars represent ± 1 *SEM*.

Figure 2-2 shows matching law analyses for individual rats. The log ratio of average left-to-right responses is plotted as a function of the log ratio of obtained alcohol deliveries for the two response alternatives. The solid lines represent least-squares regression fits of Equation 1 to the data. The sensitivity (slope) and bias (*y*-intercept) parameter values, as well as the variance accounted for by Equation 1 are located on the bottom of each panel of Figure 2-2. All matching functions have positive slopes, with sensitivity parameters ranging from 0.38 to 0.52. All slopes are significantly greater than zero, $F(1, 3)$ all > 1.55, $p = .001$ (Zar, 1999). The bias parameter was negligible for all rats, ranging from –0.06 to 0.06. The generalized matching law accounted for 98-99% of the variance in the data of individual rats.

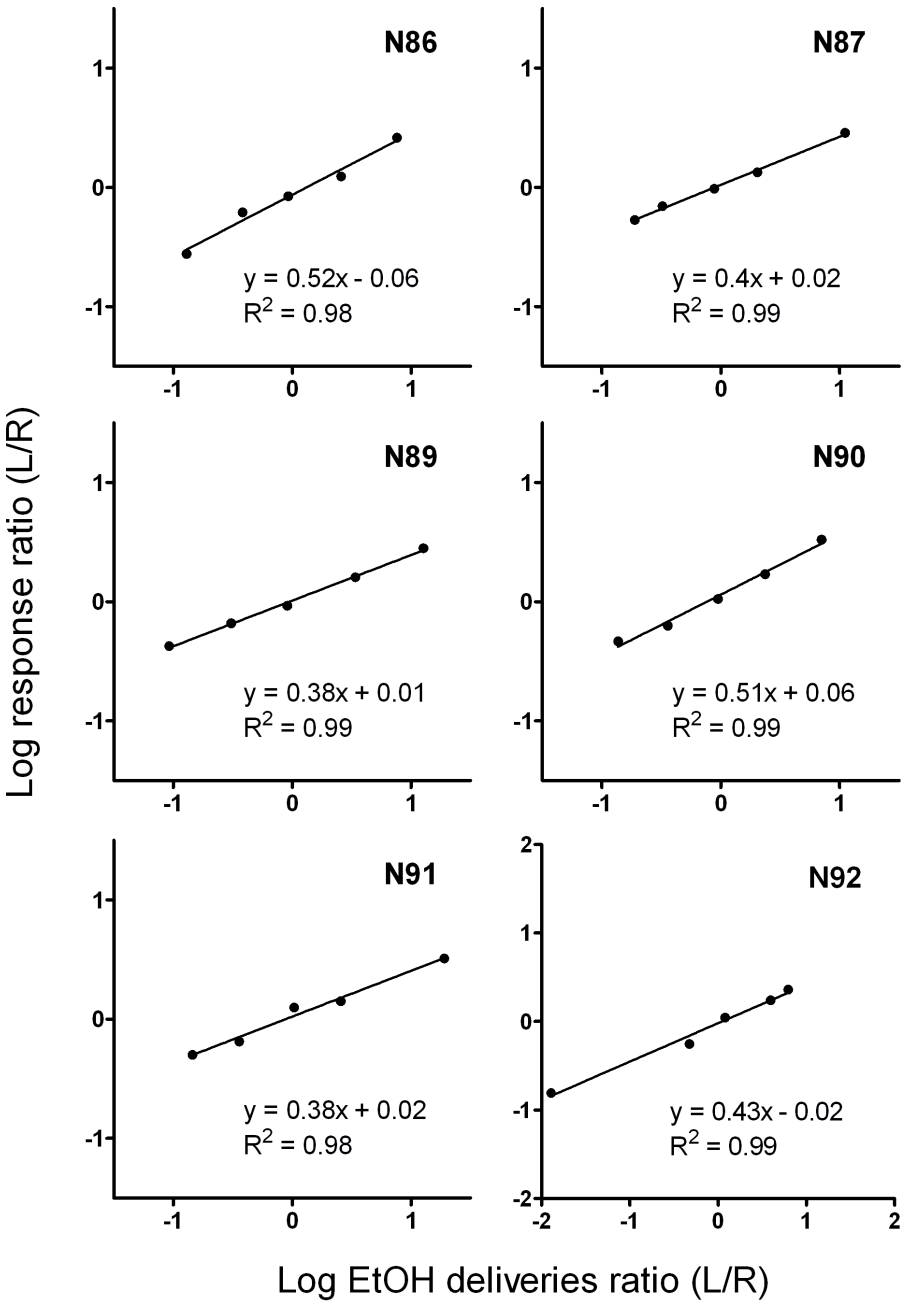

Figure 2-2. Matching functions for individual rats. Log response ratios (left/right) are plotted as a function of the log ratios of obtained alcohol deliveries (left/right). Each data point represents the average of the last 5 sessions of each condition. The solid lines are least-squares regression fits of Equation 1 to the data. The equations show the parameters of the matching function (*a* and log *b*) and the variance accounted for (R^2) by the matching law (Equation 1). Note that the axes are extended for rat N92.

Discussion

The generalized matching law accounted well for changes in the allocation of rats' behavior with changes in relative alcohol delivery rates in a free-operant choice procedure. This study extends the Martinetti and colleagues (2000, 2007) studies to a procedure more typical of generalized matching law studies and the findings suggest that the poor fits of Equation 1 reported in the Martinetti and colleagues studies were not due to the use of alcohol as a reinforcer. Further, the present findings add to the growing body of literature suggesting that quantitative accounts of operant behavior may serve as useful frameworks for the study of drug-maintained behavior (e.g., behavioral momentum theory: Jimenez-Gomez & Shahan, 2007; Shahan & Burke, 2004; generalized matching law: Woolverton, 1996).

Despite the present sensitivity values being lower than those reported in previous studies with food-maintained (i.e., 0.8; see Baum, 1979; Wearden & Burgess, 1982, for reviews) and drug-maintained responding ($a \approx 0.8$; e.g., Iglauer & Woods, 1974), the values obtained in the present experiment are comparable to those previously reported. Davison and McCarthy (1988) reanalyzed Shull and Pliskoff's (1967) data of rats responding for food on concurrent schedules and found sensitivity values of $a \approx 0.2$ with a 0.5-s COD. In the present experiment, variations in the allocations of rats' choice behavior with changes in the relative rate of alcohol delivery also were in accord with some results from generalized matching law analyses with drug reinforcers (e.g., Anderson & Woolverton, 2000, with 0.004 mg/kg/inj alfentanil as reinforcer).

Future empirical work will be required to determine if the generalized matching

law also may be valuable in the study of the conditions under which alcohol consumption is chosen over other concurrently available behaviors and the impact of treatments aimed at decreasing alcohol-maintained responding (see Vuchinich & Tucker, 1988). Although others have assessed pharmacological treatments for alcohol abuse in choice procedures (e.g., Hodge, Samson, Lewis, & Erickson, 1993; Samson & Grant, 1985; Young, Mahlev, Chi, & de Wit, 2005), future research can benefit from quantifying the specificity and effectiveness of treatments with changes in the bias and sensitivity parameters of the matching function. In addition, the usefulness of quantitative models of choice between different stimulus contexts based on the generalized matching law (e.g., contextual choice model; Grace, 1994) may prove to be a valuable tool for the study of drug-associated cues and treatments aimed at decreasing their impact on drug craving and relapse.

CHAPTER 3

CONTEXT AFFECTS PREFERENCE FOR ALCOHOL-ASSOCIATED CONDITIONED REINFORCEMENT ON CONCURRENT-CHAINS SCHEDULES [2]

Abstract

Contextual cues associated with drugs become conditioned reinforcers and play an important role in drug taking. Extensive work has been conducted using the concurrent-chains procedure to study the role of contextual variables on preference between different reinforcement contexts. The present experiments attempted to extend these findings by using the concurrent-chains procedure to examine whether the value of alcohol-associated contexts can be modulated by changes in the temporal context. In Experiment 1, rats responded on concurrent chains with equal initial-link variable-interval (VI) 10-s schedules. Across conditions, terminal-link fixed-interval schedules were varied to yield 1:1, 9:1, and 1:9 reinforcement ratios of alcohol delivery. Initial-link response rates reflected the changes in terminal-link schedules, with indifference in the 1:1 condition and preference for the rich terminal link in the other conditions. In Experiment 2, terminal-link schedules remained constant with a nine-fold reinforcement ratio while initial-link schedules were changed to VI 60 s, 10 s, and 60 s. Preference for the rich terminal link was less extreme when initial links were longer (i.e., the initial-link effect). These findings suggest that the concurrent-chains procedure could be a useful

[2] Co-authored by Corina Jimenez-Gomez and Timothy A. Shahan.

animal model for the study of alcohol-associated conditioned reinforcers and the evaluation of behavioral and pharmacological treatments aimed at decreasing the value of drug-associated contexts.

Introduction

Stimuli that accompany the delivery of drugs can acquire reinforcing value through Pavlovian associations and become conditioned reinforcers (e.g., Schuster & Woods, 1968; see also Di Chiara, 1999; Everitt & Robbins, 2005). Current theories of drug addiction suggest that drug-associated conditioned reinforcers play an important role in the maintenance and persistence of drug-taking behavior (e.g., Robinson & Berridge, 1993, 2000). In addition, drug-associated stimuli have been closely linked to drug seeking, craving, and relapse (e.g., Di Ciano & Everitt, 2003; Stewart et al., 1984, for research with animals; Lubman, Allen, Peters, & Deakin, 2007; Marissen et al., 2006, for research with humans; see also Carter & Tiffany, 1999).

Carter and Tiffany (1999) analyzed data from several cue-reactivity studies and found that drug-associated cues triggered craving and desire to consume drugs in human participants addicted to various drugs. Further, Carter and Tiffany noted that future research should focus on investigating how the interactions between contextual variables modulate drug-taking behavior. In operant conditioning research, contextual variables have been shown to determine behavior and impact the degree of conditioning (Fantino, 2001). Contextual variables include a stimulus paired with delivery of reinforcement (i.e.,

conditioned reinforcer), delay to primary reinforcement, or the availability of other sources of reinforcement.

One role of contextual variables, the temporal context, or delay to reinforcement, has been an integral aspect of current classical and operant conditioning theories. For instance, according to scalar expectancy theory (SET; Gibbon, 1977; Gibbon & Balsam, 1981), a context acquires value to the extent that it signals that the time to reinforcement is shorter than the average overall delay to reinforcement. Similarly, according to delay-reduction theory (DRT; Fantino, 1969; Squires & Fantino, 1971), a stimulus context functions as a conditioned reinforcer because it signals a reduction in time to primary reinforcement relative to the average time to reinforcement in the absence of differential stimuli. DRT has been widely used to account for the effects of the interaction of contextual variables (e.g., delay to reinforcement and value of contextual cues) on performance on a procedure commonly used when quantifying the effects of context—the concurrent-chains procedure.

In the concurrent-chains procedure, subjects choose between two concurrently available alternatives (i.e., initial links) to obtain access to one of two mutually exclusive stimulus contexts associated with primary reinforcement (i.e., terminal links; Autor, 1969; Herrnstein, 1964). The relative allocation of behavior during the initial links reflects preference for the terminal-link stimulus contexts, which function as conditioned reinforcers (e.g., Dunn et al., 1987; Moore, 1985; see Williams, 1994, for review). One basic prediction of models of concurrent-chains performance (e.g., DRT) is that preference in the initial links will change with changes in the relative delay to primary

reinforcement delivery in the terminal links. By increasing the delay to the delivery of the primary reinforcement in a terminal link, the value of the terminal-link stimulus context (i.e., conditioned reinforcer) is decreased (Squires & Fantino, 1971). This effect emphasizes the interaction between contextual variables in that the value of the stimulus context depends on the relative delay to delivery of the primary reinforcement in that context.

Another instance in which the value of a context is affected by manipulations of schedule parameters in a concurrent-chains procedure is the initial-link effect. The initial-link effect occurs when, given unequal terminal-link schedules, preference for the terminal link with a shorter delay to primary reinforcer delivery is made less extreme by increasing the length of the initial-link schedules (Fantino, 1969; see Davison & McCarthy, 1988, for review). In other words, the initial-link effect is a result of the interaction between relative delays and the overall delay to reinforcement. According to DRT, when the initial-link schedules are increased, entering the preferred terminal link will signal a relatively smaller reduction in overall time to reinforcement compared to the other terminal link than when the initial-link schedules are shorter. That is, the preferred terminal link no longer signals a greater reduction in time to delivery of the primary reinforcer and, as a result, preference for this terminal link should decrease. Thus, the initial-link effect can be interpreted as a decrease in value of the conditioned reinforcers (Squires & Fantino, 1971). Both changes in relative reinforcement delay and the initial-link effect emphasize the role of contextual variables in modulating the value of conditioned reinforcers (see Fantino, 2001).

Few studies investigating concurrent-chains performance have used rats as subjects (cf. Mazur, 2005, 2007). Furthermore, to the best of our knowledge, application of the conceptual framework provided by quantitative models of concurrent-chains performance to the study of drug-associated cues has not been pursued previously. Iglauer and Woods (1974) used the concurrent-chains procedure with a drug reinforcer, but the use of this procedure was mainly to diminish the disruptive effects of cocaine on choice behavior, not for an analysis of choice between drug-associated contexts. Extending the use of this procedure to the study of drug-associated cues may be useful because the conceptual framework provided by quantitative models of concurrent-chains performance predicts how contextual variables impact the effects of cues or conditioned reinforcers on choice behavior. The purpose of the present experiments was to extend the concurrent-chains procedure and demonstrate two robust findings – changes in preference as a function of changes in relative delay to reinforcement and the initial-link effect. Findings consistent with those from studies with non-drug reinforcers would suggest that this procedure and general framework may be a useful animal model for studying the role of drug-associated stimuli on the maintenance of drug taking.

Experiment 1

The purpose of Experiment 1 was to assess the usefulness of the concurrent-chains procedure as an animal model of choice between two contexts associated with different delays to delivery of alcohol. This experiment sought to demonstrate shifts in preference as a function of changes in the relative delay of alcohol delivery in the

terminal links by changing the interval schedule controlling alcohol deliveries, as predicted by DRT (Squires & Fantino, 1971). According to DRT, preference for the initial link associated with the terminal link in which alcohol is delivered after a shorter delay should be approximately 15-fold greater relative to the other initial link.

Method

Subjects. Five male Long Evans rats approximately 7 months old and with prior experience with alcohol self-administration in a choice procedure were used in this experiment. The rats were maintained at 80% of their free-feeding weights (320-350 g) by supplementary feeding of 12-15 g of rat chow after the daily sessions. The rats were housed individually in a temperature-controlled colony with a 12:12 hr light/dark cycle (lights on at 7:00 a.m.). Experimental sessions were conducted seven days per week during the light periods at approximately the same time every day. Water was freely available in the home cage. Animal care and housing was conducted in accordance to the standards set by the Guide for the Care and Use of Laboratory Animals (National Research Council, 1996).

Apparatus. Four Med Associates® operant conditioning chambers were used. Each chamber was approximately 30 cm long, 24 cm wide, and 21 cm high, and housed in a sound-attenuating cubicle. The back panel of each chamber was equipped with five nose pokes. Only the three center nose pokes were used in this experiment. Each nose poke hole was 2.5 cm square and 2.2 cm deep. An infrared detector was located across each nose poke unit 1.0 cm from the front. A yellow 6.4-mm diameter stimulus light was mounted flush behind the back wall of each nose poke. Each chamber contained a 28-V

DC houselight at the top center of the front panel and a solenoid-operated dipper that delivered the liquid solutions. Extraneous noise was masked by a chamber ventilation fan and white noise. Control of experimental events and data recording was conducted using Med Associates® interfacing and programming. Solutions were prepared with distilled water, table sugar, and 95% stock ethanol.

Procedures. Training was not necessary because rats had prior experience self-administering alcohol on a concurrent variable-interval (VI) VI schedule. As in previous studies of alcohol-associated cues conducted in our lab (Shahan, 2002; Shahan & Jimenez-Gomez, 2006), a 2% sucrose 10% alcohol solution was used as reinforcer in the present experiment. A 2% sucrose solution by itself does not maintain responding (Shahan, 2002).

During the initial links, the two side nose pokes were lit. A response on a side nose poke initiated the timer for the initial-link schedules. After an initial-link schedule had timed out, a response on the corresponding side nose poke extinguished the side nose poke lights and lit the center nose poke. The two terminal links were differentially signaled by a pulsing tone (0.5 s on, 0.5 s off) or steady tone. Assignment of these stimulus conditions was counterbalanced across rats. After an alcohol dipper (0.1 ml) was delivered in a terminal link the initial link stimuli were reinstated. This cycle was repeated 30 times per session. The houselight was lit during the entire session. During alcohol deliveries, all lights were extinguished and the light inside the dipper trough was lit.

Initially, concurrent VI 10 s VI 10 s (Fleshler & Hoffman, 1962) schedules were arranged in the initial links and fixed-ratio 1 was arranged in the terminal links. A 0.5-s change-over-delay (COD) was imposed for switching from one response to the other in the initial links and was timed from the first response on the changed-to alternative. The response requirement for the terminal links was gradually increased across approximately 20 sessions to fixed-interval (FI) 5 s for the first condition.

The overall rate of alcohol deliveries remained constant across conditions but the relative to delay to alcohol deliveries in the two terminal links varied as follows: 1:1 (FI 5 s FI 5 s), 9:1 (FI 1 s FI 9 s), and 1:9 (FI 9 s FI 1 s). The order in which rats were exposed to the 1:9 and 9:1 conditions was counterbalanced. All conditions lasted 15 sessions, which was sufficient to produce stability in response allocations.

Data analysis. Preference during the initial links was calculated as the logarithmic (log) ratio of absolute responses on the left relative to responses on the right nose poke. Individual subject's log preference ratios were calculated for each session and the average of the last 5 sessions of each condition were used for statistical analysis. Repeated-measures analysis of variance (ANOVA) with condition and session as within-subject variables were used to assess whether the log preference ratio significantly differed across conditions. Statistical significance was determined using $p = .05$.

Results and Discussion

Table 3-1 presents individual rats' average response rates in the initial and terminal links for the last 5 sessions of each condition. As expected, rats' initial-link response rates in the 1:1 condition were similar for both initial links (except N90 who

Table 3-1

Individual Rats' Average Response Rates During the Initial and Terminal Links for the Last Five Sessions of Each Condition of Experiment 1[a]

		N86		N87		N90		N91		N92	
Condition		L	R	L	R	L	R	L	R	L	R
1:1	IL	14.7	12.0	29.4	30.8	40.5	19.9	28.9	28.3	30.0	30.4
	TL	74.2	82.1	95.5	85.9	101.2	110.0	91.2	92.3	99.5	92.2
9:1	IL	66.4	8.4	54.0	17.3	89.1	30.7	98.0	5.6	95.2	16.8
	TL	53.1	101.6	39.9	83.5	41.6	184.5	71.9	81.0	136.0	46.5
1:9	IL	21.8	39.3	28.7	39.6	8.7	69.4	5.5	112.4	6.5	104.2
	TL	107.8	49.7	96.0	31.6	153.0	30.9	108.2	76.7	42.2	111.6

[a]Equal FI 5-s schedules were arranged in both terminal links in the 1:1 condition, FI 1-s FI 9-s schedules were arranged on the left and right terminal links in the 9:1 condition, and FI 9-s FI 1-s schedules were arranged on the left and right terminal links in the 1:9 condition.

showed a bias for the left). For all rats, response rates were higher for the initial link that lead to the terminal link delivering alcohol on a FI 1-s schedule in the 1:9 and 9:1 conditions. Hereafter, the FI 1-s schedule will be referred to as the rich terminal link and the FI 9-s schedule will be referred to as the lean terminal link. Thus, all rats preferred the rich terminal link. Terminal link response rates were similar in the 1:1 condition for all rats. Because terminal links ended with the delivery of a single reinforcer and the FI schedule in the rich terminal link was only 1-s long, only a brief amount of time was available for responding. Thus, during the 1:9 and 9:1 conditions, terminal link response rates tended to be lower in the rich terminal link. The average g/kg of alcohol delivered across conditions remained constant (Mean [*SD*] = 0.66 (0.01), 0.76 (0.01), 0.73 (0.01), 0.69 (0.01), and 0.72 (0.01) g/kg for N86, N87, N90, N91, and N92, respectively). This was expected because each terminal link entry ended with the delivery of an alcohol dipper and the same number of cycles occurred in each session.

Figure 3-1 shows individual rats' average left-to-right log preference ratio across conditions. The bottom right panel shows the mean data. According to DRT (Squires & Fantino, 1971), changes in the delay to primary reinforcer delivery during the terminal links will impact preference in the initial links. As the terminal link schedules changed across conditions, the allocation of behavior in the initial links changed to reflect preference for the rich terminal link (see Table 3-1), consistent with previous findings with food-maintained behavior (e.g., Herrnstein, 1964). The bars close to the zero line reflect indifference between the terminal link alternatives in the 1:1 condition (except for N90 who had a bias for the left lever, see Table 3-1). During the 9:1 condition, all rats preferred the left terminal link, as indicated by the bars falling above the indifference point (horizontal line). Conversely, during the 1:9 condition, all rats preferred the right terminal link, as indicated by the bars being below the indifference point. A repeated-measures ANOVA showed that the change in the log preference ratio across conditions was statistically significant, $F(2, 8) = 16.13$, $p = .002$.

Obtained preference values were similar, although somewhat less extreme than those predicted by DRT (Squires & Fantino, 1971). According to DRT, the rich-to-lean preference ratio during the 1:9 and 9:1 conditions should have been 15.55. That is, rats' preference for the initial link associated with the rich terminal link should have been approximately 15-fold relative to the lean terminal link. Rats' preference ratios, however, were 11.30 on average. As Davison and McCarthy (1988) point out, DRT consistently predicts changes in preference more extreme than those obtained (see also Fantino & Davison, 1983). In addition, Mazur (2005, 2007) has noted that rats may differ from

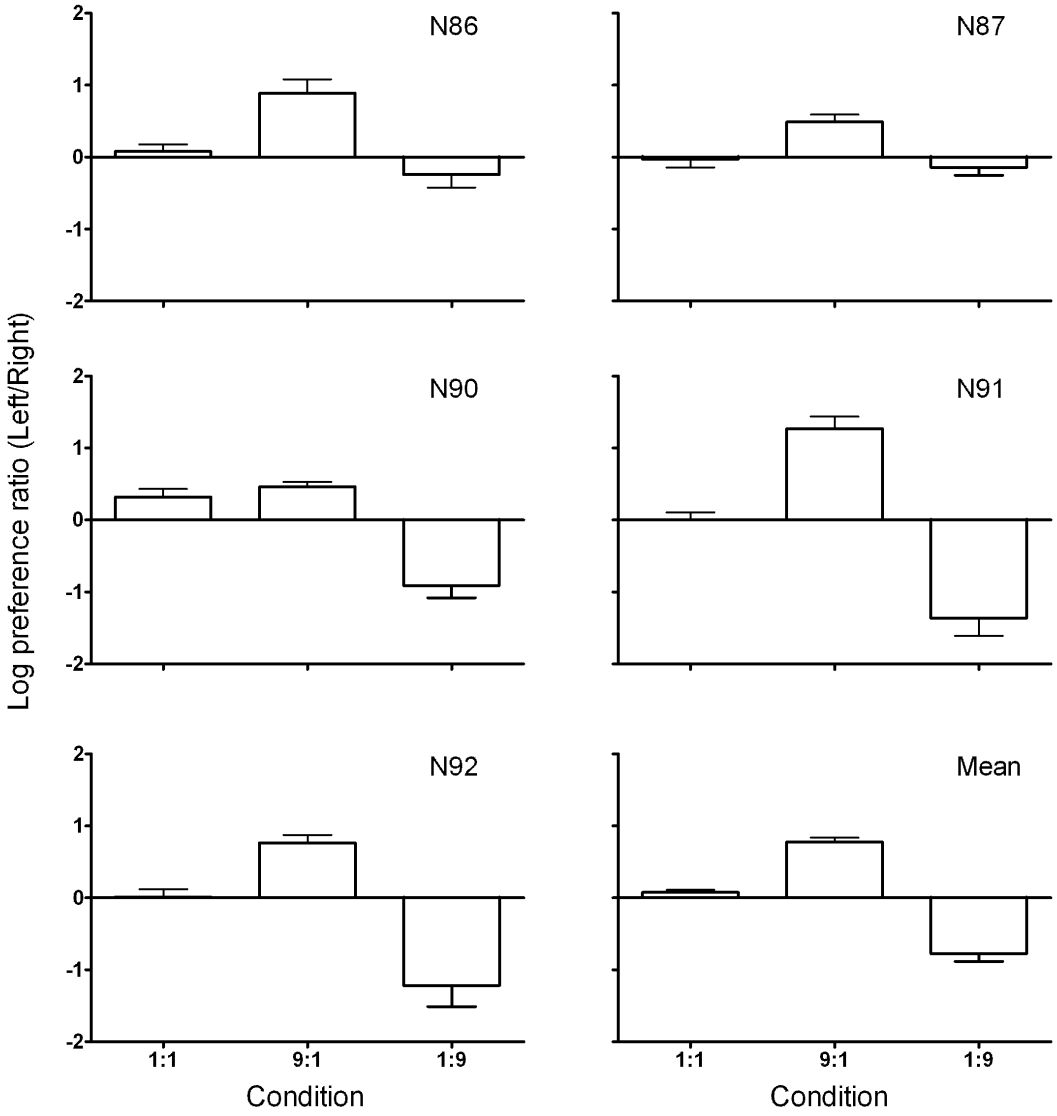

Figure 3-1. Left-to-right log preference ratio for each condition of Experiment 1. Each panel shows individual subject data. Bottom right panel shows means of all subjects. Each bar represents the average of the last five sessions of each condition. Error bars represent *SD* for individual subjects and *SEM* for mean.

pigeons on concurrent-chains performance. Specifically, Mazur found that, in adjusting-delay procedures, the presence of stimuli during the delay between the choice response and the delivery of primary reinforcers did not impact rats' preference as strongly as it impacted pigeons' behavior. Despite the discrepancies between the specific model predictions and the obtained results, the findings of this experiment suggest that the concurrent-chains procedure and the conceptual framework provided by models of concurrent-chains performance may be useful tools for the study of alcohol-associated stimulus contexts.

The present experiment extended the use of the concurrent-chains procedure to the study of alcohol-associated conditioned reinforcement. Rats' preference changed with changes in the relative rate of alcohol deliveries in the terminal links, consistent with the general prediction of DRT (Squires & Fantino, 1971) and previous studies of concurrent-chains performance of food-maintained responding (Herrnstein, 1964; see Davison & McCarthy, 1988; Williams, 1988, for reviews). This finding suggests that the concurrent-chains procedure may be a useful animal model of choice between contexts differentially associated with drug reinforcers. Experiment 1 showed that changes in the delay to alcohol delivery in the terminal links affected the value of the terminal link stimulus context. Another way in which the value of the context can be impacted is by increasing the initial-links schedules (i.e., initial-link effect).

Experiment 2

The initial-link effect refers to a decrease in preference with increases in the

initial-links schedules (Fantino, 1969). The initial-link effect is a well-established finding in concurrent-chains performance (see Davison & McCarthy, 1988; Mazur, 2001; Williams, 1988, for reviews); however, this effect has not been replicated with rats or with drug-maintained behavior. The purpose of Experiment 2 was to extend the initial-link effect to rats responding for alcohol reinforcers. An important aspect of this finding is that it would suggest that the value of stimuli associated with the availability or delivery of a drug is modulated by contextual variables. This, in turn, would suggest that the value of drug-associated cues is subject to change.

In Experiment 2, rats responded for an alcohol solution on a concurrent-chains procedure with equal initial-links schedules and a nine-fold difference in relative delays to alcohol deliveries across two terminal links. Initial-links schedules were varied across conditions from VI 60 s to VI 10 s to assess whether preference for the terminal link delivering alcohol after a shorter delay would decrease (i.e., initial-link effect). According to DRT, preference for the side that leads to the rich terminal link during the short initial links (VI 10 s) condition should be 15-fold greater than preference for the side that leads to the lean terminal link, whereas during longer initial links (VI 60 s) preference only should be 1.5-fold greater.

Method

Subjects and apparatus. The same rats and apparatus as in Experiment 1 were used. Between Experiment 1 and this experiment, the rats experienced short-term exposures to different initial-link schedule values in an attempt to identify parameters for

this experiment. As in Experiment 1, a 2% sucrose 10% alcohol solution was used as a reinforcer.

Procedures. The first condition arranged VI 60 s initial links and FI 1 s FI 9 s terminal links. Rats N86, N87, and N91 had the FI 1 s and FI 9 s assigned to the right and left terminal links, respectively. Rats N90 and N92 had the opposite assignment. During the initial links, the two side nose pokes were lit and a response on a side nose poke initiated the initial link timers. After the initial link schedules timed out, a response on the corresponding side nose poke extinguished the side nose poke lights and lit the center nose poke. The two terminal links were differentially signaled by a pulsing tone (0.5 s on, 0.5 s off) or steady tone, counterbalanced across rats. During alcohol deliveries, all lights were extinguished and the light inside the dipper trough was lit. Initial-link stimuli were reinstated after an alcohol dipper was delivered in the terminal link. This cycle was repeated 30 times per session. If rats did not complete all the cycles, the session ended after 60 min. This limit on session duration was needed only for rat N92 during the first few sessions of the VI 60-s initial link conditions. After 15 sessions of the initial condition, initial-link schedules were decreased to VI 10 s. Finally, initial-link schedules were returned to VI 60 s. As in Experiment 1, all conditions lasted 15 sessions.

Data analysis. Preference during the initial links was calculated as the log ratio of absolute response on the initial link that lead to the rich terminal link relative to responses on the initial link that lead to the lean terminal link. As in Experiment 1, a log preference ratio was calculated for each session and the average of the last five sessions of each condition were used for statistical analysis with repeated-measures ANOVA.

Results and Discussion

Table 3-2 presents individual rats' average response rates in the initial and terminal links for the last 5 sessions of each condition. For all rats, initial-link response rates were higher on the side leading to the rich terminal link across all conditions. When the initial-link schedule was decreased to VI 10 s, initial-link response rates on the side that lead to the rich terminal link increased, whereas response rates on the side that lead to the lean terminal link decreased. When the initial-link schedule was returned to the initial value of VI 60 s, initial-link response rates on the side that lead to the rich and lean terminal links decreased and increased, respectively. For all rats, terminal-link response rates were higher during the lean terminal link across all conditions. Because all terminal link presentations ended with the delivery of alcohol and the rich terminal link was only 1-s long, terminal link response rates tended to be lower in the rich terminal link. As in Experiment 1, the average g/kg of alcohol delivered across conditions remained constant (0.66, 0.76, 0.72, 0.69, and 0.71 g/kg for N86, N87, N90, N91, and N92, respectively).

Table 3-2

Individual Rats' Average Response Rates During the Initial and Terminal Links for the Last Five Sessions of Each Condition of Experiment 2

		N86		N87		N90		N91		N92	
Condition		FI 9 s	FI 1 s	FI 9 s	FI 1 s	FI 1 s	FI 9 s	FI 9 s	FI 1 s	FI 1 s	FI 9 s
VI 60 IL	IL	6.1	36.5	11.2	40.0	98.1	30.0	14.1	51.9	60.6	7.4
	TL	73.9	37.2	74.4	29.8	28.3	136.5	94.6	64.4	35.3	73.9
VI 10 IL	IL	1.8	97.4	7.6	65.5	142.5	3.8	4.9	125.2	126.1	5.8
	TL	72.3	38.5	77.6	33.1	40.2	150.4	79.8	75.6	38.7	74.0
VI 60 IL	IL	1.8	32.8	7.1	30.3	91.4	11.1	8.7	45.5	37.7	8.0
	TL	65.6	51.1	78.0	28.9	32.4	154.0	80.3	75.4	37.5	52.7

Figure 3-2 shows individual rats' average rich-to-lean log preference ratio across conditions and the bottom right panel shows the mean data. During the VI 10-s condition, preference for the rich terminal link increased relative to the previous condition, as indicated by the higher middle bars in each panel of Figure 3-2. Preference for the rich terminal link was less extreme for all rats during both VI 60-s conditions (side bars in each panel of Figure 3-2). A repeated-measures ANOVA showed that the change in the log preference ratio across conditions was statistically significant, $F(2, 8) = 19.76$, $p = .001$.

As in Experiment 1, the general direction of the effect was in accordance with DRT (Squires & Fantino, 1971), but the obtained preference values were not accurately predicted. According to DRT, the rich-to-lean preference ratio during the VI 60-s and VI 10-s conditions should have been 1.49 and 15.55, respectively. Rats' preference ratios, however, were on average 6.43 and 35.99, respectively. As Davison and McCarthy (1988) point out, DRT does not always accurately predict changes in preference. Overall, the direction of the obtained effects in the present experiment was accurately predicted and consistent with previous findings (see Davison & McCarthy). Thus, study of alcohol-associated cues within the concurrent chains framework can benefit from the general predictive validity of quantitative models such as DRT.

The most relevant aspect of Experiment 2 was the demonstration that the value of a preferred alcohol-associated context could be decreased. Although the initial-link effect is a well-established finding of concurrent-chains performance (e.g., Davison & McCarthy, 1988; Mazur, 2001; Williams, 1988), to the best of our knowledge, no studies

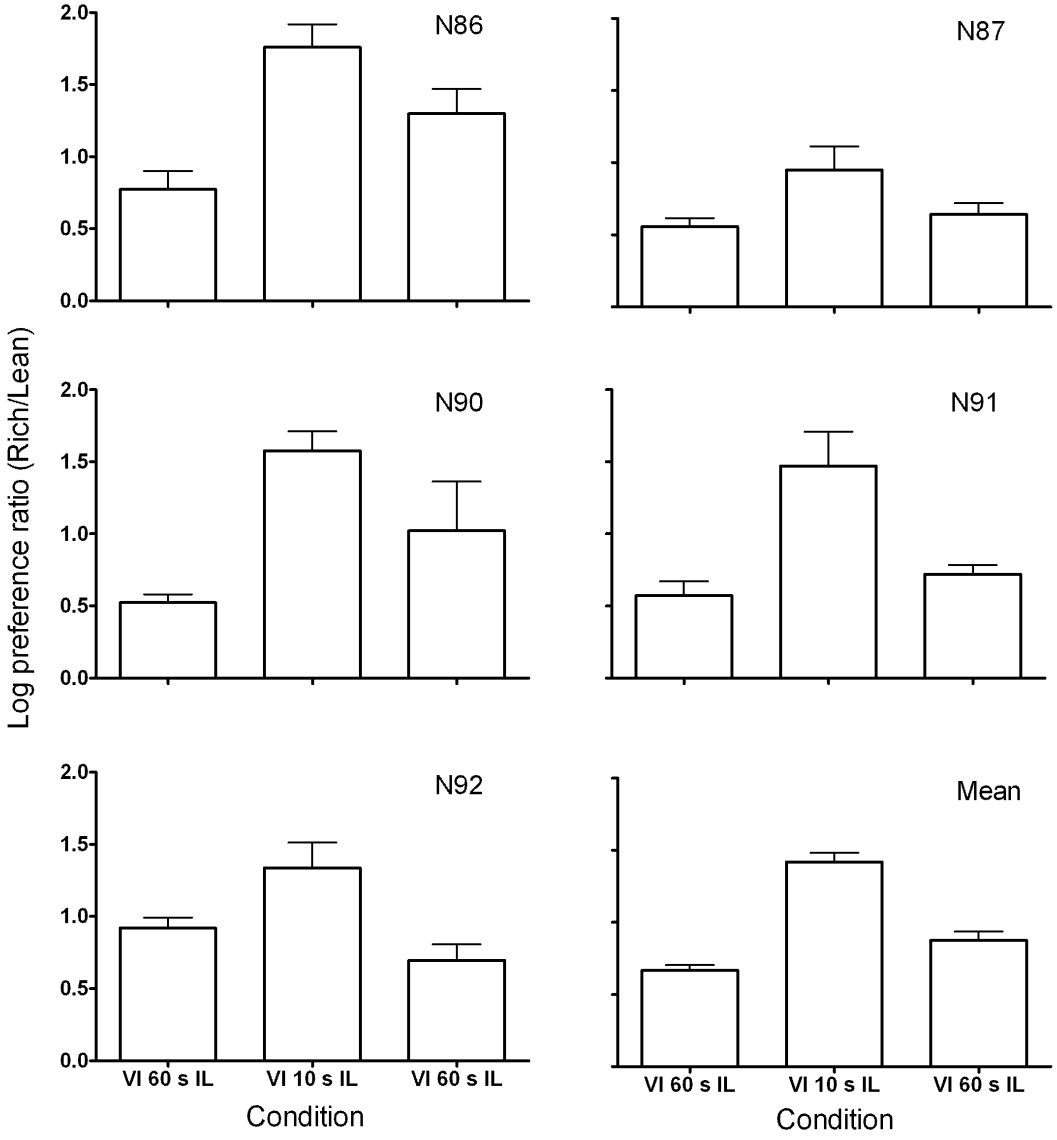

Figure 3-2. Rich-to-lean log preference ratio for each condition of Experiment 2. Each panel shows individual subject data. Bottom right panel shows means of all subjects. Each bar represents the average of the last five sessions of each condition. Error bars represent *SD* for individual subjects and *SEM* for mean.

have shown this effect with rats or behavior maintained by drug reinforcers. The present experiment constitutes the first demonstration of the initial-link effect with rats and with alcohol as a primary reinforcer. Demonstration of the initial-link effect with alcohol-maintained responding is the first step in assessing contextual manipulations aimed at decreasing preference for stimulus contexts associated with drugs.

General Discussion

The concurrent-chains procedure has been widely used to study conditioned reinforcement (see Davison & McCarthy, 1988, for review). Most research using concurrent chains and testing predictions of quantitative models of concurrent-chains performance has used pigeons responding for food reinforcement. In the present experiments, rats responded for access to two contexts associated with different delays to alcohol delivery. All rats showed a preference for the context associated with the delivery of alcohol after a shorter delay (i.e., rich terminal link) and preference decreased as a function of increases in initial-links schedules (i.e., initial-link effect). These findings are consistent with previous studies of concurrent-chains performance of food-maintained responding (Herrnstein, 1964; see Davison & McCarthy, 1988; Williams, 1988, for reviews) and suggest that rats' responding on concurrent chains fit with the general predictions of a well-established quantitative model of concurrent-chains performance (i.e., DRT; Squires & Fantino, 1971). In addition, this constitutes the first demonstration that these findings extend to drug-maintained responding. Thus, the concurrent-chains procedure provides a novel animal model for the study of drug-associated conditioned

reinforcement. Related findings using this procedure with food-maintained behavior can be used to inform researchers about the role of alcohol-associated cues and can guide future research. For instance, this procedure lends itself to the analysis of both preference for and the persistence of behavior in a particular stimulus context.

In humans, drug abuse and dependence are characterized by persistent patterns of drug seeking and taking behaviors (American Psychiatric Association, 1994). Research with animals has shown that the resistance to change or persistence of alcohol-maintained behavior depends on the same contextual variables (e.g., rate of reinforcement in the context) as food-maintained behavior (Jimenez-Gomez & Shahan, 2007; Shahan & Burke, 2004). These findings suggest that contextual variables have general effects on drug-maintained behavior that should be considered in understanding drug abuse and dependence. Preference in concurrent-chains schedules and the persistence of behavior under conditions of disruption (e.g., extinction, satiation) have been suggested to be indices of the underlying strength of behavior (e.g., Grace & Nevin, 1997; see Nevin & Grace, 2000, for review). Just as preference for a terminal-link stimulus context can be interpreted as indicative of the value of the context, it can be used to predict how persistent behavior would be in that stimulus context. In addition to providing a useful framework for the study of the value of drug-associated contexts, the concurrent-chains procedure and models of concurrent-chains performance allow for the assessment of the response-strengthening effects of drug reinforcers in those contexts. Given that drug-associated contexts play a key role in triggering drug craving and relapse in humans (e.g., Carter & Tiffany, 1999; Marissen et al., 2006) and make drug seeking and taking more

persistent, further study of the interaction between contextual variables and the persistence of drug taking is warranted.

In Experiment 2, the finding that preference for the rich context became more or less extreme with changes in the initial-link schedules suggests that the value of drug-associated cues is modulated by contextual variables (e.g., temporal context), consistent with SET (Gibbon, 1977; Gibbon & Balsam, 1981) and DRT (Fantino, 1969; Squires & Fantino, 1971). A direction for future research is the study of the effect of access to a context with cues associated to a nondrug reinforcer (e.g., food, sex) on preference for the context associated with a drug reinforcer. Carroll and colleagues have shown that concurrent availability of nondrug reinforcers decreases self-administration of phencyclidine (Carroll, 1985), alcohol (Carroll, Rodefer, & Rawleigh, 1995), and cocaine (Comer, Hunt, & Carroll, 1994). Similarly, Nader and Woolverton (1991, 1992a, 1992b) have shown that variables such as the magnitude of the alternative nondrug reinforcers impact the degree to which drug self-administration is suppressed (see also Campbell & Carroll, 2000). It is possible that concurrent availability of access to contexts associated with nondrug reinforcers also could decrease drug self-administration and the value of drug-associated cues. For instance, a concurrent-chains procedure with one initial link leading to a drug context and another leading to a nondrug context (e.g., presence of food) could be used to study the effects of various environmental manipulations (e.g., rate of food delivery) on preference for the drug context. In addition, by increasing the initial-link schedules it may be possible to shift preference for a drug-associated context to preference for a context associated with nondrug reinforcers. The present experiments

suggest that the concurrent-chains procedure provides a useful animal model for the study of the contextual variables that modulate preference for a drug context. Therefore, the concurrent-chains procedure could be useful in the assessment of behavioral and pharmacological treatments aimed at decreasing drug taking, craving, and relapse.

CHAPTER 4

SUMMARY AND CONCLUSIONS

Although alcohol-maintained behavior has been widely studied, quantitative models of choice and conditioned reinforcement have not been systematically applied to behavior maintained by alcohol. The few studies that have been conducted (Martinetti et al., 2000, 2007) have obtained results that deviate from the typical findings of matching-law studies. Thus, the purpose of the present series of experiments was to test the generality of the matching law with alcohol as a reinforcer and extend the conceptual framework provided by quantitative models of choice in concurrent and concurrent-chains schedules to behavior maintained by alcohol and alcohol-associated cues.

In the first experiment (Chapter 2), rats responded for an alcohol solution on a concurrent schedule of reinforcement and relative rates of reinforcement were varied across conditions. This manipulation allowed for estimates of the bias and sensitivity parameters of the generalized matching law. Overall, the matching law provided a good description of changes in rats' relative allocation of behavior with changes in the relative rate of alcohol delivery. These findings suggest that the atypical findings reported by Martinetti and colleagues (2000, 2007) likely were a result of the two-bottle choice procedures used and not the use of alcohol as a reinforcer. Consequently, the generalized matching law may be a useful tool in the study of alcohol-related choice. Furthermore, as suggested by Vuchinich and Tucker (1988), the general framework provided by choice research in the field of operant conditioning can provide an interesting and useful way to conceptualize alcohol-taking behavior. Vuchinich and Tucker noted that behavioral

theories of choice could be particularly useful in understanding the environmental conditions under which alcohol drinking emerges as a preferred behavior.

In humans, alcohol and drug abuse can be conceptualized as a choice between taking a drug and engaging in other, more socially desirable behaviors (e.g., going to work, interacting with friends and family, participating in recreational activities; see APA, 1994). Choice procedures are particularly useful for the study of the effectiveness of pharmacological treatments because these procedures allow the concurrent assessment of the impact of treatments on alcohol drinking and an alternative nondrug-related behavior (see de Wit & Johanson, 1987, for review). For instance, mecamylamine, a nicotinic receptor antagonist, decreases alcohol drinking in alcohol-preferring rats (Rezvani, Overstreet, & Janowsky, 1990; cf. Dyr, Koros, Bienkowski, & Kostowski, 1999; Katner, McBride, Lumeng, Li, & Murphy, 1997). This finding suggests that mecamylamine may serve as a pharmacological treatment for alcohol abuse and dependence. One concern with pharmacological treatments in general, however, is the specificity of their actions. That is, whether the pharmacological agent selectively impacts the target behavior or it also impacts other behaviors or processes. For instance, mecamylamine decreases food intake in rats (Dyr et al.) and has mood-altering effects in human participants (Shytle, Silver, & Sanberg, 2000; Shytle, Silver, Sheehan, Sheehan, & Sanberg, 2002; Silver, Shytle, & Sanberg, 2000). Therefore, before declaring the usefulness of a pharmacological agent for the treatment of alcohol or drug abuse, it is important to examine whether other behaviors also will be impacted. Choice procedures are well suited for this assessment.

Young and colleagues (2005) used a choice procedure to test the effects of mecamylamine on preference for alcohol in healthy social drinkers. Participants were exposed to a procedure in which they could choose between alcohol and various amounts of money. Their findings showed that the effects of mecamylamine were specific to choice for alcohol. The Young and colleagues' study highlights the usefulness of choice procedures in the study of pharmacological treatments for alcohol abuse and dependence. Similarly, Samson and colleagues have assessed the effects of pharmacotherapies on rats' alcohol self-administration in the presence of concurrently available water or sucrose (e.g., Hodge, Samson, Lewis, & Erickson, 1993; Samson & Grant, 1985). For instance, Samson and Grant showed that the effects of chlordiazepoxide on alcohol self-administration differed depending on what type of reinforcer was concurrently available (water or sucrose). Thus, the use of a choice procedure allowed for the identification of contextual variables that alter the effectiveness of potential pharmacotherapies.

Future studies could benefit from inclusion of the conceptual framework of the generalized matching law in understanding the relative impact pharmacological treatments have on choice for alcohol over other nondrug alternatives. As mentioned in Chapter 1, fitting the generalized matching law equation allows one to derive sensitivity and bias parameters. Sensitivity refers to how closely the allocation of behavior across response alternatives matches the relative allocation of reinforcement, whereas bias refers to preference for a response alternative irrespective of the relative rate of reinforcement delivered by each response alternative. These parameters can provide quantitative indices of the specificity of the pharmacological treatment. For instance, a treatment that biases

behavior towards a nondrug alternative may be more desirable than one that simply decreases responding in general, because this treatment could help the individual come into contact with other sources of reinforcement rather than just decreasing overall levels of activity. Furthermore, these parameters also could provide quantitative means of comparing the effectiveness of different pharmacological treatments in preclinical research.

The second and third experiments (Chapter 3) extended the use of the concurrent-chains procedure to rats responding for access to stimulus contexts associated with different delays to alcohol delivery. These experiments examined the concurrent-chains procedure for use as a novel animal model for the study of drug-associated cues. Furthermore, the predictions of DRT, a widely used quantitative model of concurrent-chains performance, were used to assess the impact of environmental manipulations aimed at modulating the value of alcohol-associated contexts. First, results showed that choice between two contexts depended on the different delays to alcohol delivery in each context (Experiment 1, Chapter 3). That is, all rats preferred the context with a shorter delay to alcohol delivery. Second, when the initial-link schedules were increased (Experiment 2, Chapter 3), preference for the rich context decreased, as predicted by DRT (Squires & Fantino, 1971). Thus, these findings that are common with food-maintained behavior were demonstrated with rats responding for alcohol. Together, these findings suggest that the value of alcohol-associated cues can be modulated by contextual variables.

The findings from the experiments in Chapter 3 were analyzed within the

framework of DRT because this is the most widely used model of concurrent-chains performance. In addition, this model is the most parsimonious (i.e., no free parameters) in accounting for the behavioral phenomena studied in these experiments. Future studies could use other models of concurrent-chains performance (e.g., contextual-choice model, Grace, 1994) that include free parameters to derive sensitivity and bias parameters, as with the generalized matching law. These parameters could serve as quantitative indices of the impact of behavioral or pharmacological manipulations aimed at decreasing choice for a context associated with drugs. For instance, when the initial-links schedules are increased, sensitivity to the relative delays to reinforcement may decrease. Similarly, pharmacological treatments may impact sensitivity to relative delays to drug delivery and, as a result, the sensitivity to the relative value of drug-associated contexts.

The importance of showing the initial-link effect with rats responding for alcohol is that it suggests that the value of environmental cues associated with the availability and/or delivery of drugs may be modified. Relatedly, Fantino (2001) suggested that the overall context in which a behavior occurs modulates choice behavior and the value of reinforcers and conditioned reinforcers delivered in that context (see O'Daly, Meyer, & Fantino, 2005, for related findings). Thus, the role context plays in modulating drug-taking behavior and the value of drug-associated conditioned reinforcers should be considered. Models of concurrent-chains performance include the modulating role of the context in choice for conditioned reinforcers, and thus, may serve as a general framework for the study of the role of drug-associated cues in drug-taking behavior. As stated in Chapter 1, the concurrent-chains procedure is the standard method for studying

conditioned reinforcement because it allows for a quantitative analysis of the determinants of the value of the conditioned reinforcer. The present experiments showed that the concurrent-chains procedure could be a useful animal model for the study of drug-associated conditioned reinforcement.

Although animal models may not fully capture the complexity of human behavior, animal models of drug addiction have been useful in predicting the abuse liability of new drugs, investigating neurological mechanisms underlying drug addiction, and assessing the role of environmental stimuli in drug taking (see Cardinal & Everitt, 2004; Everitt, Dickinson, & Robbins, 2001; Gardner, 2000; Pickens, Meisch, & Thompson, 1978; Shippenberg & Koob, 2002; Willner, 1997, for reviews). According to Willner and to Shippenberg and Koob, animal models are useful for understanding human drug abuse to the extent that they have face validity, construct validity, and predictive validity. Face validity refers to the similarity between the model and the actual human phenomena (e.g., similar route of administration), whereas construct validity refers to the theoretical rationale for the model and how it relates to human phenomena. When using the framework of quantitative models of choice, it is possible to derive measures (e.g., bias parameter from generalized matching law) or general predictions of changes in behavior resulting from contextual manipulations (e.g., initial-link effect) that can provide information about how contextual variables that modulate operant behavior in general also can impact alcohol-maintained behavior in both animals and humans. Therefore, the framework provided by these procedures and quantitative models could enhance the construct validity of animal models of behavior maintained by alcohol and alcohol-

associated cues to the extent that they can inform the researcher about the underlying behavioral process in human drug abuse.

The predictive validity of an animal model refers to how accurately the findings with the animal model can be translated back to the human condition. More specifically, predictive validity refers to the extent to which the animal model allows researchers to make predictions about human behavior (e.g., drug taking). In order for animal models of drug taking and choice for drug contexts to have greater predictive validity, translational research must be conducted to confirm that the findings with animals also apply to humans. According to Shippenberg and Koob (2002), future study of drug addiction requires that animal models have predictive validity if they are to contribute to our understanding of the underlying behavioral and neurobiological processes. Although this is an important step, it is beyond the scope of the present experiments and no conclusions regarding predictive validity or direct applications to humans can be made. However, future research could evaluate the predictive validity of this animal model by using the theoretical framework provided by quantitative models of choice to guide translational research.

Given the role drug-associated cues play in drug craving and relapse, evaluating the effectiveness of treatments aimed at decreasing the reinforcing value of drug-associated cues also may be an important direction for future research. The concurrent-chains procedure and models of concurrent-chains performance provide methods for quantitatively examining and comparing the effectiveness of behavioral and pharmacological treatments aimed at decreasing drug taking and the value of drug-

associated cues in animal models of drug self-administration. As a potential behavioral treatment, the impact of access to a nondrug context on the value of a drug-associated context could be assessed with animals responding on the concurrent-chains procedure. Carroll and colleagues have shown that concurrent availability of non-drug reinforcers decreases self-administration of a variety of drugs (e.g., Carroll, 1985; Carroll et al., 1995; Comer et al., 1994). An important and interesting next step would be to assess how manipulating access to a context associated with a non-drug reinforcer modifies the value of drug-associated cues in animal models of drug taking.

The concurrent-chains procedure also may be useful in examining the effectiveness of potential pharmacological treatments aimed at decreasing drug taking and the value of contexts associated with drugs. For instance, dopamine D_3 receptors have been found to modulate the reinforcing properties of alcohol (Heidbreder et al., 2004; Russell, McBride, Lumeng, Li, & Murphy, 1996; Silvestre, O'Neill, Fernandez, & Palacios, 1996), the development of physical dependence on alcohol (Narita, Soma, Tamaki, Narita, & Suzuki, 2002), and cue-induced relapse of alcohol seeking (Marcon, Andreoli, Pilla, Tessari, & Heidbreder, 2003; Vengeliene et al., 2006; see Heidbreder et al., 2005; Newman, Grundt, & Nader, 2005, for reviews). Vengeliene and colleagues reported that long-term alcohol consumption lead to an upregulation of the expression of the dopamine D_3 receptors in the striatum of alcohol-preferring and nonselected Wistar rats, which may contribute to increased alcohol seeking and relapse behaviors. Using animal models of drug seeking and relapse, Vengliene and colleagues found that the selective dopamine D_3 receptor antagonist SB-277011-A (1, 3, 10 mg/kg) and the partial

agonist BP 897 (0.1, 1, 3 mg/kg) dose-dependently decreased alcohol seeking and relapse. Relatedly, a single administration of 30 mg/kg of SB-277011-A significantly reduces the number of alcohol reinforcers earned and the amount of alcohol consumed by treated rats and mice compared to vehicle-control subjects in alcohol self-administration procedures (see Heidbreder et al., 2005, for review). Thus, one direction to explore is whether the dopamine D_3 receptor antagonist SB-277011-A also selectively modulates preference for alcohol-associated cues or contexts. As noted above, an important consideration regarding pharmacological treatments of drug abuse is whether their effects are specific to the target behavior. Therefore, exploring whether pharmacological agents that selectively block dopamine D_3 receptors only impact choice for a context associated with alcohol would be an important step in determining the usefulness of these compounds in the treatment of alcohol abuse and dependence.

The present series of experiments provide support for the use of the framework provided by quantitative models of choice behavior and choice procedures as animal models for the study of behavior maintained by alcohol and alcohol-associated cues, as well as behavior maintained by other drugs. The use of concurrent and concurrent-chains schedules can be useful animal models for preclinical research assessing behavioral and pharmacological treatments aimed at decreasing alcohol taking and the value of cues or contexts associated with alcohol.

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Woolverton, W. L., & Alling, K. (1999). Choice under concurrent VI schedules: Comparison of behavior maintained by cocaine or food. *Psychopharmacology, 141*, 47-56.

Woolverton, W. L., & Anderson, K. G. (2006). Effects of delay to reinforcement on the choice between cocaine and food in rhesus monkeys. *Psychopharmacology, 186*, 99-106.

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CURRICULUM VITAE

Corina Jimenez-Gomez

PERSONAL INFORMATION

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Birth date:	January 23, 1978		
Birthplace:	Caracas, Venezuela		

EDUCATIONAL HISTORY

Present	*Doctoral candidate*	Department of Psychology Utah State University Logan, UT
2005	*Master of Science*	Department of Psychology Utah State University Logan, UT

Master's Thesis - Resistance to change of ethanol self-administration: Effects of naltrexone and extinction.
Advisor: Timothy A. Shahan, Ph.D.

2002	*License in Psychology*	Department of Psychology Universidad Católica Andrés Bello Caracas, Venezuela

Undergraduate Thesis - Effects of the delay of reinforcement and the strain of the rat (Wistar Kyoto and Spontaneously Hypertensive Rats) on the performance under a multiple schedule.
Advisor: Cristina Vargas-Irwin, Ph.D.

AWARDS AND HONORS

2008	College of Education and Human Services 1st Place Presentation in Graduate Research Symposium

2007-2008	Department of Psychology. Utah State University Walter R. Borg Scholarship: Scholarship and Research Productivity Award
2007	College of Education and Human Services 1st Place Presentation in Graduate Research Symposium
2007	Utah State University Women and Gender Research Institute Graduate Travel Award
2006 – 2009	Student Representative to the Association for Behavior Analysis Executive Council
2006 – 2007	Program Representative for Behavior Analysis program at Utah State University to the Association for Behavior Analysis
2005 – 2007	Society for the Advancement of Behavior Analysis student presenter grant
1997 and 1998	Special Aknowlegment to Outstanding UCABista Student Universidad Católica Andrés Bello (UCAB). Caracas, Venezuela
1993	Finalist of the 18th Venezuelan Mathematics Olympics and member of the Venezuelan team for the Iberoamerican Mathematics Olympics. Caracas, Venezuela

POSITIONS HELD

2007 – present	*Graduate Instructor* "Scientific Thinking and Methods in Psychology" Department of Psychology, Utah State University Supervisor: Scott Bates, Ph.D.
Fall 2006	*Graduate Teaching Assistant* Department of Psychology, Utah State University Supervisor: Scott Bates, Ph.D.
2004 – present	*Behavior Analysis Laboratory Manager* Department of Psychology, Utah State University
2003 – 2006	*Graduate Research Assistant* Department of Psychology, Utah State University Supervisor: Timothy A. Shahan, Ph.D.

2001 – 2002	*Undergraduate Teaching Assistant* Department of Psychology, Universidad Católica Andrés Bello Laboratory Instructor: Experimental Psychology Supervisor: Gustavo Peña Torbay, Ph.D.
1999 – 2002	*Undergraduate Research Assistant* Operant and Classical Conditioning Laboratory, Universidad Central de Venezuela Supervisor: Cristina Vargas-Irwin, Ph.D.

PUBLICATIONS

Refereed Articles in Print

Jimenez-Gomez, C., & Shahan, T. A. (2007). Resistance to Change of Alcohol Self-Administration: Effects of Alcohol-Delivery Rate on Disruption by Extinction and Naltrexone. *Behavioural Pharmacology, 18*, 161-169.

Podlesnik, C. A., Jimenez-Gomez, C., & Shahan, T. A. (2006). Reinstatement of Ethanol-Maintained Responding by Discontinuing Reinforcement for an Alternative Non-Drug Reinforcer: A Novel Model of Drug Relapse. *Behavioural Pharmacology, 17*, 369-374.

Shahan, T. A., & Jimenez-Gomez, C. (2006). Effects of Self-Administered Alcohol Concentration on the Frequency and Persistence of Rats' Attending to Alcohol Stimuli. *Behavioural Pharmacology*, *17*, 201-211.

Shahan, T. A., Podlesnik, C. A., & Jimenez-Gomez, C. (2006). Matching and Conditioned Reinforcement Rate. *Journal of the Experimental Analysis of Behavior*, *85*, 167-180.

Podlesnik, C. A., Jimenez-Gomez, C., Ward, R. D., & Shahan, T. A. (2006). Resistance to Change of Responding Maintained by Unsignaled Delays to Reinforcement: A Response-Bout Analysis. *Journal of the Experimental Analysis of Behavior*, *85*, 329-347.

Refereed Articles in Press

Jimenez-Gomez, C., & Shahan, T. A. Matching Law Analysis of Rats' Alcohol Self-Administration in a Free-Operant Choice Procedure. *Behavioural Pharmacology.*

Manuscripts submitted

Nevin, J. A., Ward, R. D., Jimenez-Gomez, C., Odum, A. L., & Shahan, T. A. *Differential outcomes enhance accuracy of delayed matching to sample but not resistance to change.*

Manuscripts in preparation

Jimenez-Gomez, C., & Shahan, T. A. *Context affects preference for alcohol-associated conditioned reinforcement on concurrent-chains schedules.*

Jimenez-Gomez, C., Podlesnik, C. A., & Shahan, T. A. *The effects of initial-link duration on preference and resistance to change.*

Jimenez-Gomez, C., & Shahan, T. A. *Relative resistance to change of alcohol-maintained responding of rats depends on disruptor type.*

Jimenez-Gomez, C., & Shahan, T. A. *Preference and resistance to change of responding on concurrent schedules of reinforcement.*

PRESENTATIONS AT PROFESSIONAL MEETINGS

Jimenez-Gomez, C. (2008, April). *Context Affects Preference for Alcohol-Associated Cues.* Paper presented at the 11th Annual Intermountain Paper and Poster Symposium, Logan, UT.

Jimenez-Gomez, C. & Shahan, T. A. (2007, May). *Differential Resistance to Change of Alcohol Self-Administration of Rats Depends on Type of Disruptor.* Poster session presented at the 33rd annual meeting of the Association for Behavior Analysis, San Diego, California.

McFeron, S., Jimenez-Gomez, C., & Shahan, T. A. (2007, May). Behavioral momentum of cocaine self-administration. In T. Wade-Galuska (Chair), *Quantitative Analyses in Behavioral Pharmacology: Studies of Choice, Behavioral Momentum, and Self-Control.* Symposium conducted at the 33rd annual meeting of the Association for Behavior Analysis, San Diego, California.

Odum, A., Ward, R. D., Jimenez-Gomez, C., & Shahan, T. A. (2007, May). Persistence of Accuracy and Response Rate in Delayed Matching-to-Sample with Differential Outcomes. In J. A. Nevin (Chair), *Conditional Discriminations: Conceptual Issues and New Findings.* Symposium conducted at the 33rd annual meeting of the Association for Behavior Analysis, San Diego, California.

Jimenez-Gomez, C. (2007, April). *Relative resistance to change of alcohol-maintained responding of rats depends on disruptor type.* Paper presented at the 10th Annual Intermountain Paper and Poster Symposium, Logan, UT.

Jimenez-Gomez, C., & Shahan, T. A. (2007, February). *Relative resistance to change of alcohol-maintained responding of rats depends on disruptor type.* Paper presented at the Winter Conference on Animal Learning and Behavior, Winter Park, Colorado.

Jimenez-Gomez, C., & Shahan, T. A. (2006, May). *Persistence of rats' attending to alcohol stimuli associated with different concentrations of alcohol.* Poster session presented at the 32nd annual meeting of the Association for Behavior Analysis, Atlanta, Georgia.

Podlesnik, C. A., Jimenez-Gomez, C., & Shahan, T. A. (2006, May). *Resurgence as an alternative model of drug relapse.* Poster session presented at the 32nd annual meeting of the Association for Behavior Analysis, Atlanta, Georgia.

Jimenez-Gomez, C., & Shahan, T. A. (2005, May). Resistance to change of ethanol self-administration: Effects of behavioral and pharmacological disruptors. In A. Odum (Chair), *Ethanol self-administration.* Symposium conducted at the 31st annual meeting of the Association for Behavior Analysis, Chicago, Illinois.

Jimenez-Gomez, C., Podlesnik, C. A., & Shahan, T. A. (2005, May). *Sensitivity to relative conditioned-reinforcement rate without changes in primary-reinforcement rate*. Poster session presented at the annual meeting of the Society f or the Quantitative Analysis of Behavior, Chicago, Illinois.

Podlesnik, C. A., Jimenez-Gomez, C., Ward, R., & Shahan, T. A. (2005, May). *The response-reinforcer relation in resistance to change: Effects of immediate, briefly-delayed, and longer-delayed reinforcement.* Poster session presented at the 31st annual meeting of the Association for Behavior Analysis, Chicago, Illinois.

Shahan, T. A., Podlesnik, C. A., & Jimenez-Gomez, C. (2004, July). Observing, attending, behavioral momentum, and the matching law. In R. Pitts (Chair), *Celebrating B.F. Skinner's 100th Birthday: Conditioned Reinforcement.* Symposium conducted at the 112th annual meeting of the American Psychological Association, Honolulu, Hawaii.

Jimenez-Gomez, C., Burke, K. A., & Shahan, T. A. (2004, May). *Alternative non-drug reinforcement decreases drug-maintained responding but increases resistance to change.* Poster session presented at the 30th annual meeting of the Association for Behavior Analysis, Boston, Massachusetts.

Jimenez-Gomez, C. (2002, May). *Effects of the delay of reinforcement and the strain of the rat (Wistar Kyoto and Spontaneously Hypertensive Rats) on the performance under a multiple schedule.* Paper accepted at the 28th annual meeting of the Association for Behavior Analysis, Toronto, Canada.

Jimenez-Gomez, C. & Vargas-Irwin, C. (2001, May). *Multiple schedule performance differences between Wistar Kyoto and Spontaneous Hypertensive Rats.* Poster session presented at the 27th annual meeting of the Association for Behavior Analysis, New Orleans, Louisiana.

Jimenez-Gomez, C., & Vargas-Irwin, C. (2000, November). *Performance differences between Wistar Kyoto and Spontaneous Hypertensive Rats*. Paper presented at the 50th annual meeting of the Asociación Venezolana para el Avance de la Ciencia (ASOVAC) [Venezuelan Association for the Advancement of Science], Caracas, Venezuela.

Events chaired at professional meetings

Koob, G. F. (2007, May). *The Neurobiology of Alcoholism: A Dysregulated Neuroadaptational View.* Invited address at the 33rd annual meeting of the Association for Behavior Analysis, San Diego, California.

Grace, R. C. (2007, May). *Professional Development Series: Introductory Series on Quantitative Analysis of Behavior.* Invited address at the 33rd annual meeting of the Association for Behavior Analysis, San Diego, California.

RESEARCH INTERESTS

Experimental analysis of behavior; Quantitative models of choice; The role of drug-associated cues in the maintenance of drug seeking and behavioral manipulations to decrease the value of drug cues; The persistence of operant behavior; The relation between resistance to change and preference.

MEMBERSHIP IN PROFESSIONAL ORGANIZATIONS

Association for Behavior Analysis
Society for the Quantitative Analyses of Behavior

PROFESSIONAL POSITIONS

2001 – 2002	*Psychological Counseling – individual and group psychotherapy service for college population (10h/week)* Center for Assessment and Human Development. Universidad Católica Andrés Bello. Caracas, Venezuela
Feb. 2002 – July 2002	*Clinical Psychology – psychological evaluation, diagnosis, and psychotherapy for child and adult outpatient clients (10h/week)* Psychology Unit. Social Community Center Padre Manuel Aguirre, sj. Caracas, Venezuela
Oct. 2001 – Feb. 2002	*Clinical Psychology – psychological evaluation, diagnosis, and psychotherapy for adolescent and adult inpatient and outpatient clients (10 h/week)* Department of Psychiatry and Clinical Psychology. Military Hospital “Dr. Carlos Arvelo”. Caracas, Venezuela

2000 – 2001 *School Psychology – psychological evaluation, diagnosis, and treatment of children with learning disabilities and school-related psychological problems, both individually and on a group level (5 h/week)*
Public School "Los Naranjos". La Vega, Caracas, Venezuela

2000 – 2001 *Adult and Child Psychopathology – psychological evaluation and diagnosis of hospitalized adult patients and children with developmental disabilities in educational settings (5 h/week)*
Department of Psychiatry and Clinical Psychology.
Clinical University Hospital. Universidad Central de Venezuela.
Caracas, Venezuela

2000 – 2001 *Industrial Psychology – organizational development, project management, and time management (10 h/week)*
Institute of Psychology. Universidad Central de Venezuela.
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REFERENCES

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